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(FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
L1          802 S (KOSZINOWSKI, ?)/IN,AU
L2          537 S (MESSERLE, ?)/IN,AU
L3         5359 S (BRUNE, ?)/IN,AU
L4        43708 S (HAHN, ?)/IN,AU
L5            7 S L1 AND L2 AND L3 AND L4
L6            3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7        50178 S L1 OR L2 OR L3 OR L4
L8         5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9        16997 S BAC OR L8
L10      381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11         387 S L8 AND L10
L12          82 S L11 AND L7
L13       27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14         207 S L13 AND L8
L15          60 S L14 AND L7
L16          24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17          22 S L12 NOT L15
L18          12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19         305 S L11 NOT L12
L20           5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
L21           2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)
L22       33498 S (MOSS, ?)/IN,AU OR  (DOMI, ?)/IN,AU
L23           0 S L19 AND L22
L24         557 S L9 AND L10
L25          93 S L24 AND L7
L26          11 S L25 NOT L12
L27           4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)
L28           0 S L22 AND L24
L29         464 S L24 NOT L25
L30        3618 S (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU
L31           7 S L30 AND L29
L32           4 DUPLICATE REMOVE L31 (3 DUPLICATES REMOVED)
L33           7 S L24 AND L30
L34        6767 S (DELECLUSE, ?)/IN,AU OR (HILSENDEGEN, ?)/IN,AU OR (PICH, ?)/I
L35           4 S L34 AND L24
L36           1 DUPLICATE REMOVE L35 (3 DUPLICATES REMOVED)
L37          55 S  (HAMMERSCHMIDT, ?)/IN,AU AND ((BRIELMEIER, ?)/IN,AU OR (KILG
L38          34 S L37 AND L10
L39          24 S L38 AND PY<1999
L40          14 DUPLICATE REMOVE L39 (10 DUPLICATES REMOVED)
L41        2043 S (STAVROPOULOS, ?)/IN,AU OR (STRATHDEE, ?)/IN,AU
L42          14 S (STAVROPOULOS, ?)/IN,AU AND (STRATHDEE, ?)/IN,AU
L43           4 S L41 AND L24
L44           1 DUPLICATE REMOVE L43 (3 DUPLICATES REMOVED)
L45          39 S L41 AND L10
L46          35 S L45 NOT L43
L47          18 DUPLICATE REMOVE L46 (17 DUPLICATES REMOVED)
L48          55 S L8 AND ADENOVIR?
L49           0 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L4

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                   STN Express with Discover!
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 NEWS  5  NOV 30   PHAR reloaded with additional data
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 NEWS  7  DEC 09   12 databases to be removed from STN on December 31, 2004
 NEWS  8  DEC 15   MEDLINE update schedule for December 2004
 NEWS  9  DEC 17   ELCOM reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  10 DEC 17   COMPUAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  11 DEC 17   SOLIDSTATE reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  12 DEC 17   CERAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  13 DEC 17   THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
 NEWS  14 DEC 30   EPFULL: New patent full text database to be available on STN
 NEWS  15 DEC 30   CAPLUS - PATENT COVERAGE EXPANDED
 NEWS  16 JAN 03   No connect-hour charges in EPFULL during January and
                   February 2005
 NEWS  17 JAN 26   CA/CAPLUS - Expanded patent coverage to include the Russian
                   Agency for Patents and Trademarks (ROSPATENT)

 NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

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=> S (KOSZINOWSKI, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L1          802 (KOSZINOWSKI, ?)/IN,AU

=> S (MESSERLE, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L2          537 (MESSERLE, ?)/IN,AU

=> S (BRUNE, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L3         5359 (BRUNE, ?)/IN,AU

=> S (HAHN, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L4        43708 (HAHN, ?)/IN,AU

=> S L1 AND L2 AND L3 AND L4
L5            7 L1 AND L2 AND L3 AND L4

=> DUPLICATE REMOVE L5
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L5
L6            3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)

=> D IBIB AB L6 1,2,3

L6   ANSWER 1 OF 3  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation.  on STN
ACCESSION NUMBER:   2002:253098  BIOSIS
DOCUMENT NUMBER:    PREV200200253098
TITLE:              Cytomegalovirus bacterial artificial chromosomes: A new
                    herpesvirus vector approach.
AUTHOR(S):          Messerle, Martin [Reprint author]; Hahn,
                    Gabriele [Reprint author]; Brune, Wolfram
                    [Reprint author]; Koszinowski, Ulrich H. [Reprint
                    author]
CORPORATE SOURCE:   Max von Pettenkofer Institute for Hygiene and Medical
                    Microbiology, Ludwig-Maximilians-Univeristy of Munich,
                    Pettenkofer-Strasse 9a, 80336, Munich, Germany
SOURCE:             Maramorosch, Karl [Editor]; Murphy, Frederick A. [Editor];
                    Shatkin, Aaron J. [Editor]. Adv. Virus Res., (2000) pp.
                    463-478. Advances in Virus Research. print.
```

Publisher: Academic Press Inc., 525 B Street, Suite 1900, San Diego, CA, 92101-4495, USA; Academic Press Ltd., 24-28 Oval Road, London, NW1 7DX, UK. Series: Advances in Virus Research.
CODEN: AVREA8. ISSN: 0065-3527. ISBN: 0-12-039855-9 (cloth).
DOCUMENT TYPE: Book
Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002

L6 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2000429895 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10933677
TITLE: Fast screening procedures for random transposon libraries of cloned herpesvirus genomes: mutational analysis of human cytomegalovirus envelope glycoprotein genes.
AUTHOR: Hobom U; **Brune W; Messerle M; Hahn G; Koszinowski U H**
CORPORATE SOURCE: Lehrstuhl fur Virologie, Max von Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, 80336 Munich, Germany.
SOURCE: Journal of virology, (2000 Sep) 74 (17) 7720-9.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914

AB We have cloned the human cytomegalovirus (HCMV) genome as an infectious bacterial artificial chromosome (BAC) in Escherichia coli. Here, we have subjected the HCMV BAC to random transposon (Tn) mutagenesis using a Tn1721-derived insertion sequence and have provided the conditions for excision of the BAC cassette. We report on a fast and efficient screening procedure for a Tn insertion library. Bacterial clones containing randomly mutated full-length HCMV genomes were transferred into 96-well microtiter plates. A PCR screening method based on two Tn primers and one primer specific for the desired genomic position of the Tn insertion was established. Within three consecutive rounds of PCR a Tn insertion of interest can be assigned to a specific bacterial clone. We applied this method to retrieve mutants of HCMV envelope glycoprotein genes. To determine the infectivities of the mutant HCMV genomes, the DNA of the identified BACs was transfected into permissive fibroblasts. In contrast to BACs with mutations in the genes coding for gB, gH, gL, and gM, which did not yield infectious virus, BACs with disruptions of open reading frame UL4 (gp48) or UL74 (gO) were viable, although gO-deficient viruses showed a severe growth deficit. Thus, gO (UL74), a component of the glycoprotein complex III, is dispensable for viral growth. We conclude that our approach of PCR screening for Tn insertions will greatly facilitate the functional analysis of herpesvirus genomes.

L6 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001201984 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11050952
TITLE: Cytomegalovirus bacterial artificial chromosomes: a new herpesvirus vector approach.
AUTHOR: **Messerle M; Hahn G; Brune W; Koszinowski U H**
CORPORATE SOURCE: Department of Virology, Ludwig-Maximilians-University of Munich, Germany.

```
SOURCE:             Advances in virus research, (2000) 55 463-78.  Ref: 76
                    Journal code: 0370441. ISSN: 0065-3527.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    General Review; (REVIEW)
                    (REVIEW, TUTORIAL)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200104
ENTRY DATE:         Entered STN: 20010417
                    Last Updated on STN: 20010417
                    Entered Medline: 20010412


=> D HIS

     (FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
L1           802 S (KOSZINOWSKI, ?)/IN,AU
L2           537 S (MESSERLE, ?)/IN,AU
L3          5359 S (BRUNE, ?)/IN,AU
L4         43708 S (HAHN, ?)/IN,AU
L5             7 S L1 AND L2 AND L3 AND L4
L6             3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)

=> S L1 OR L2 OR L3 OR L4
L7         50178 L1 OR L2 OR L3 OR L4

=> S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L8          5817 (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)

=> S BAC OR L8
L9         16997 BAC OR L8

=> S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYTOMEGALOVIR? OR
CMV? OR HSV? OR ADENOVIR? OR VARICELLA?)
L10       381914 (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYTOME
                 GALOVIR? OR CMV? OR HSV? OR ADENOVIR? OR VARICELLA?)

=> S L8 AND L10
L11          387 L8 AND L10

=> S L11 AND L7
L12           82 L11 AND L7

=> D HIS

     (FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
L1           802 S (KOSZINOWSKI, ?)/IN,AU
L2           537 S (MESSERLE, ?)/IN,AU
L3          5359 S (BRUNE, ?)/IN,AU
L4         43708 S (HAHN, ?)/IN,AU
L5             7 S L1 AND L2 AND L3 AND L4
L6             3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7         50178 S L1 OR L2 OR L3 OR L4
L8          5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9         16997 S BAC OR L8
L10       381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11          387 S L8 AND L10
L12           82 S L11 AND L7
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=> S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L13      27515 (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10

=> S L13 AND L8
L14        207 L13 AND L8

=> S L14 AND L7
L15         60 L14 AND L7

=> DUPLICATE REMOVE L15
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L15
L16          24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)

=> D IBIB AB L16 1-24

L16  ANSWER 1 OF 24     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2004319470     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15220454
TITLE:              SUMOylation of the human cytomegalovirus 72-kilodalton IE1
                    protein facilitates expression of the 86-kilodalton IE2
                    protein and promotes viral replication.
AUTHOR:             Nevels Michael; Brune Wolfram; Shenk Thomas
CORPORATE SOURCE:   Department of Molecular Biology, Princeton University,
                    Princeton, NJ 08544-1014, USA.
CONTRACT NUMBER:    CA85786 (NCI)
SOURCE:             Journal of virology, (2004 Jul) 78 (14) 7803-12.
                    Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200408
ENTRY DATE:         Entered STN: 20040629
                    Last Updated on STN: 20040804
                    Entered Medline: 20040803
AB   The 72-kDa immediate-early 1 protein (IE1-72kDa) of human cytomegalovirus
     has been previously shown to be posttranslationally modified by covalent
     conjugation to the ubiquitin-related protein SUMO-1.  Using an
     infectious bacterial artificial
     chromosome clone of human cytomegalovirus, we
     constructed a mutant virus (BADpmIE1-K450R) that is deficient for
     SUMOylation of IE1-72 kDa due to a single amino acid exchange in the
     SUMO-1 attachment site.  Compared to wild-type virus, this mutant grew
     more slowly and generated a reduced yield in infected human fibroblasts,
     indicating that SUMO modification is required for the full activity of
     IE1-72 kDa.  The lack of SUMOylation did not affect the intranuclear
     localization of IE1-72 kDa, including its ability to target to and disrupt
     PML bodies and to bind to mitotic chromatin.  Likewise,
     SUMOylation-deficient IE1-72 kDa activated several viral promoters as
     efficiently as the wild-type protein.  However, the failure to modify
     IE1-72 kDa resulted in substantially reduced levels of the IE2 transcript
     and its 86-kDa protein (IE2-86 kDa).  These observations suggest that SUMO
     modification of IE1-72 kDa contributes to efficient HCMV replication by
     promoting the accumulation of IE2-86 kDa.

L16  ANSWER 2 OF 24     MEDLINE on STN                    DUPLICATE 2
ACCESSION NUMBER:   2004457377     IN-PROCESS
DOCUMENT NUMBER:    PubMed ID: 15364458
TITLE:              Cloning of the varicella-zoster virus
                    genome as an infectious bacterial
                    artificial chromosome in Escherichia
                    coli.
```

AUTHOR: Nagaike Kazuhiro; Mori Yasuko; Gomi Yasuyuki; Yoshii Hironori; Takahashi Michiaki; Wagner Markus; **Koszinowski Ulrich**; Yamanishi Koichi
CORPORATE SOURCE: Department of Microbiology, Osaka University Graduate School of Medicine, 2-2 Yamada-oka, Suita, Osaka 565-0871, Japan.
SOURCE: Vaccine, (2004 Sep 28) 22 (29-30) 4069-74. Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20040915
Last Updated on STN: 20041219

AB The **complete genome** of the **varicella**-zoster virus (VZV) Oka strain has been cloned as a **bacterial artificial chromosome** (BAC). Following electroporation into Escherichia coli (E. coli) strain DH10B, the VZV BAC was stably propagated over multiple generations of its host. Human embryonic lung (HEL) cells transfected with VZV BAC DNA recovered from DH10B showed cytopathic effect (CPE), and virus spread to neighbouring cells was observed. BAC vector sequences are flanked by loxP sites and, coinfection of the reconstituted virus, with a recombinant adenovirus expressing Cre recombinase removed the bacterial sequences. The resulting recombinant rV02 grew as well as the parental virus in HEL cells. The recombinant VZV will promote VZV research and increase use of the viral genome as an investigative tool.

L16 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:360964 CAPLUS
DOCUMENT NUMBER: 141:83186
TITLE: Cloning of β-herpesvirus genomes as bacterial artificial chromosomes
AUTHOR(S): Borst, Eva-Maria; Crnkovic-Mertens, Irena; **Messerle, Martin**
CORPORATE SOURCE: Virus Cell Interaction Unit, Medical Faculty, Martin-Luther University, Halle-Wittenberg, Germany
SOURCE: Methods in Molecular Biology (Totowa, NJ, United States) (2004), 256(Bacterial Artificial Chromosomes, Volume 2), 221-239
CODEN: MMBIED; ISSN: 1064-3745
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A completely new approach for the construction of **herpesvirus** mutants that is based on cloning of the virus **genome** as a **bacterial artificial chromosome** (BAC) in Escherichia coli was developed. The procedures for the insertion of the BAC vector sequences into the viral genome, for isolation of circular genome intermediates from infected cells and for transformation and propagation of the BACs in E. coli are described. Protocols for the isolation of BACs from bacteria, for characterization of BACs by restriction enzyme digestion and for reconstitution of recombinant viruses by transfection of BACs into permissive cells are given.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 24 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 3
ACCESSION NUMBER: 2004:78605 BIOSIS
DOCUMENT NUMBER: PREV200400081120
TITLE: Coding potential of laboratory and clinical strains of human cytomegalovirus.
AUTHOR(S): Murphy, Eain; Yu, Dong; Grimwood, Jane; Schmutz, Jeremy;

Dickson, Mark; Jarvis, Michael A.; **Hahn, Gabriele** ; Nelson, Jay A.; Myers, Richard M.; Shenk, Thomas E. [Reprint Author]

CORPORATE SOURCE: Department of Molecular Biology, Princeton University, Princeton, NJ, 80544, USA
tshenk@molbio.princeton.edu

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (December 9 2003) Vol. 100, No. 25, pp. 14976-14981. print.
ISSN: 0027-8424 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: DDBJ-AC146851; EMBL-AC146851; GenBank-AC146851; DDBJ-AC146904; EMBL-AC146904; GenBank-AC146904; DDBJ-AC146905; EMBL-AC146905; GenBank-AC146905; DDBJ-AC146906; EMBL-AC146906; GenBank-AC146906; DDBJ-AC146907; EMBL-AC146907; GenBank-AC146907; DDBJ-AC146999; EMBL-AC146999; GenBank-AC146999
ENTRY DATE: Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004

AB Six strains of human cytomegalovirus have been sequenced, including two laboratory strains (AD169 and Towne) that have been extensively passaged in fibroblasts and four clinical isolates that have been passaged to a limited extent in the laboratory (Toledo, FIX, PH, and TR). All of the sequenced viral genomes have been cloned as infectious bacterial artificial chromosomes. A total of 252 ORFs with the potential to encode proteins have been identified that are conserved in all four clinical isolates of the virus. Multiple sequence alignments revealed substantial variation in the amino acid sequences encoded by many of the conserved ORFs.

L16 ANSWER 5 OF 24 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2003328231 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12857893

TITLE: Vaccination of mice with bacteria carrying a cloned **herpesvirus genome** reconstituted in vivo.

AUTHOR: Cicin-Sain Luka; **Brune Wolfram**; Bubic Ivan; Jonjic Stipan; **Koszinowski Ulrich H**
CORPORATE SOURCE: Max von Pettenkofer Institute, LMU, Munich, Germany.

SOURCE: Journal of virology, (2003 Aug) 77 (15) 8249-55.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030715
Last Updated on STN: 20030820
Entered Medline: 20030819

AB Bacterial delivery systems are gaining increasing interest as potential vaccination vectors to deliver either proteins or nucleic acids for gene expression in the recipient. Bacterial delivery systems for gene expression in vivo usually contain small multicopy plasmids. We have shown before that **bacteria** containing a herpesvirus **bacterial artificial chromosome** (BAC) can reconstitute the virus replication cycle after cocultivation with fibroblasts in vitro. In this study we addressed the question of whether bacteria containing a single plasmid with a complete viral genome can also reconstitute the viral replication process in vivo. We used a natural mouse pathogen, the murine **cytomegalovirus** (MCMV), whose **genome** has previously been cloned as a BAC in Escherichia coli. In this study, we tested a new application for BAC-cloned herpesvirus genomes. We show that the MCMV BAC can be stably maintained in certain strains of Salmonella enterica serovar Typhimurium as well and that both

serovar Typhimurium and E. coli harboring the single-copy MCMV BAC can reconstitute a virus infection upon injection into mice. By this procedure, a productive virus infection is regenerated only in immunocompromised mice. Virus reconstitution in vivo causes elevated titers of specific anti-MCMV antibodies, protection against lethal MCMV challenge, and strong expression of additional genes introduced into the viral genome. Thus, the reconstitution of infectious virus from live attenuated bacteria presents a novel concept for multivalent virus vaccines launched from bacterial vectors.

L16 ANSWER 6 OF 24 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2003073629 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12584345
TITLE: An essential role of the enhancer for murine cytomegalovirus in vivo growth and pathogenesis.
AUTHOR: Ghazal Peter; **Messerle Martin**; Osborn Kent; Angulo Ana
CORPORATE SOURCE: Department of Immunology, The Scripps Research Institute, La Jolla, California 92037, USA.
CONTRACT NUMBER: AI-30627 (NIAID)
AI-44851 (NIAID)
SOURCE: Journal of virology, (2003 Mar) 77 (5) 3217-28.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030214
Last Updated on STN: 20030321
Entered Medline: 20030320

AB The transcription of cytomegalovirus (CMV) immediate-early (IE) genes is regulated by a large and complex enhancer containing an array of binding sites for a variety of cellular transcription factors. Previously, using **bacterial artificial chromosome** recombinants of the virus **genome**, it was reported that the enhancer region of murine **CMV** (MCMV) is dispensable but performs a key function for viral multiplication (A. Angulo, M. Messerle, U. H. Koszinowski, and P. Ghazal, J. Virol. 72:8502-8509, 1998). In the present study, we defined, through the reconstitution of infectious enhancerless MCMVs, the growth requirement for the enhancer in tissue culture and explored its significance for steering a productive infection in vivo. A comparison of cis and trans complementation systems for infection of enhancerless virus in permissive fibroblasts revealed a multiplicity-dependent growth phenotype that is severely compromised in the rate of infectious-virus multiplication. The in vivo impact of viruses that have an amputated enhancer was investigated in an extremely sensitive model of MCMV infection, the SCID mouse. Histological examination of spleens, livers, lungs, and salivary glands from animals infected with enhancer-deficient MCMV demonstrated an absence of tissue damage associated with CMV infection. The lack of pathogenic lesions correlated with a defect in replication competence. Enhancerless viruses were not detectable in major target organs harvested from SCID mice. The pathogenesis and growth defect reverted upon restoration of the enhancer. Markedly, while SCID mice infected with 5 PFU of parental MCMV died within 50 days postinfection, all mice infected with enhancerless virus survived for the duration of the experiment (1 year) after infection with 5 x 10(5) PFU. Together, these results clarify the importance of the enhancer for MCMV growth in cell culture and underscore the in vivo significance of this region for MCMV virulence and pathogenesis.

L16 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:473689 CAPLUS
DOCUMENT NUMBER: 140:13448

TITLE: Herpesvirus-BACs: New tools for molecular medicine
AUTHOR(S): Borst, Eva; **Messerle, Martin**
CORPORATE SOURCE: AG Virus-Zell-Interaktion Zentrum fuer Angewandte Medizinische und Humanbiologische Forschung (ZAMED) Medizinische Fakultaet, Universitaet Halle-Wittenberg, Halle, D-06120, Germany
SOURCE: Bioforum (2003), 26(5), 284-285
CODEN: BFRME3; ISSN: 0940-0079
PUBLISHER: GIT Verlag GmbH & Co. KG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review is given on human **herpesviruses**, **genome** products, conventional mutagenesis of **herpesviruses**, and **bacterial artificial chromosome** (BAC)-cloning and mutagenesis of **herpesviruses**. Construction of virus mutants by reverse genetics, therapeutical application of herpesvirus gene products, and perspectives in research on herpesvirus pathogenesis and development of vaccines and vectors for gene therapy are discussed.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:231442 CAPLUS
DOCUMENT NUMBER: 139:18067
TITLE: Cloning of the genomes of human cytomegalovirus strains Toledo, TownevarRIT3, and Townelong as BACs and site-directed mutagenesis using a PCR-based technique
AUTHOR(S): **Hahn, Gabriele**; Rose, Dietlind; Wagner, Markus; Rhiel, Sylvia; McVoy, Michael A.
CORPORATE SOURCE: Abteilung Virologie, Max von Pettenkofer Institut, Ludwig-Maximilians-Universitt, Munchen, D-80336, Germany
SOURCE: Virology (2003), 307(1), 164-177
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 230-kb human **cytomegalovirus genome** is among the largest of the known viruses. Expts. to determine the genetic determinants of attenuation, pathogenesis, and tissue tropism are underway; however, a lack of complete sequence data for multiple strains and substantial problems with genetic instability during in vitro propagation create serious complications for such studies. For example, recent findings suggest that common laboratory strains Towne and AD169 passaged in cultured human fibroblasts are missing up to 15 kb of genetic information relative to clin. isolates. To establish standard, genetically stable genomes that can be sequenced, disseminated, and repeatedly reconstituted to produce virus stocks, the authors have undertaken to clone two variants of Towne, designated Townelong and Towneshort (referred to as TownevarRIT3) (A., Proc. Natl. Acad. Sci. USA 98, 7829-7834), and the pathogenic strain Toledo into bacterial artificial chromosomes (BACs). The authors further demonstrate the ease with which mutagenesis can be achieved by deleting 13.5 kb from the Toledo genome using a PCR-based technique.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 24 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003114047 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12627394
TITLE: Cloning of herpesviral genomes as bacterial artificial chromosomes.
AUTHOR: Adler Heiko; **Messerle Martin**; **Koszinowski Ulrich H**

CORPORATE SOURCE: GSF-Research Center for Environment and Health, Institute of Molecular Immunology, Clinical Cooperation Group Hematopoietic Cell Transplantation, Munich, Germany.. h.adler@gsf.de
SOURCE: Reviews in medical virology, (2003 Mar-Apr) 13 (2) 111-21. Ref: 58
Journal code: 9112448. ISSN: 1052-9276.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030311
Last Updated on STN: 20030426
Entered Medline: 20030425

AB Herpesviruses, which are important pathogens for both animals and humans, have large and complex genomes with a coding capacity for up to 225 open reading frames (ORFs). Due to the large **genome** size and the slow replication kinetics in vitro of some **herpesviruses**, mutagenesis of viral genes in the context of the viral **genome** by conventional recombination methods in cell culture has been difficult. Given that mutagenesis of viral genes is the basic strategy to investigate function, many of the herpesvirus ORFs could not be defined functionally. Recently, a completely new approach for the construction of **herpesvirus** mutants has been developed, based on cloning of the virus **genome** as a **bacterial artificial chromosome** (BAC) in E. coli. This technique allows the maintenance of viral genomes as a plasmid in E. coli and the reconstitution of viral progeny by transfection of the BAC plasmid into eukaryotic cells. Any genetic modification of the viral **genome** in E. coli using prokaryotic recombination proteins is possible, thereby allowing the generation of mutant viruses and facilitating the analysis of **herpesvirus** genomes cloned as **infectious** BACs. In this review, we describe the principle of cloning a viral genome as a BAC using murine gammaherpesvirus 68 (MHV-68), a mouse model for gammaherpesvirus infections, as an example.

L16 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:658249 CAPLUS
DOCUMENT NUMBER: 137:196683
TITLE: Expression vectors for the propagation of **infectious** human **cytomegalovirus** genomes retaining wild-type characteristics of clinical isolates
INVENTOR(S): **Hahn, Gabriele**
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066629	A2	20020829	WO 2002-EP1867	20020221
WO 2002066629	C1	20030227		
WO 2002066629	A3	20031009		
WO 2002066629	C2	20040115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2438322	AA	20020829	CA 2002-2438322		20020221
EP 1368465	A2	20031210	EP 2002-716799		20020221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
US 2004087001	A1	20040506	US 2002-275287		20021113
PRIORITY APPLN. INFO.:			EP 2001-104171	A	20010221
			EP 2001-116044	A	20010702
			WO 2002-EP1867	W	20020221

AB Vectors containing genomes of human **cytomegalovirus** (HCMV) that can be used to propagate **infectious** virus particles that retain phenotypic characteristics of a clin. virus isolate, including the ability to grow on endothelial cells and to induce microfusion, are described. Such vectors can be used e.g. for production of reconstituted HCMV virus retaining the phenotypic characteristics of a parental clin. isolate and for studying genes and functions of genes of HCMV virus. A further aspect are mutant viruses and inter alia their use for studying aspects of infectivity of HCMV virus. Cloning of genomes of clin. isolates of HCMV cultured in human vascular endothelial cells by homologous recombination with a BAC vector is demonstrated. The cloned genome was replicated in MRC-5 cells transformed with the BAC. Viruses retained the cell tropism of the original isolate. A series of deletion mutants were generated by PCR to identify the genes essential for cell tropism.

L16 ANSWER 11 OF 24 EMBASE on STN

ACCESSION NUMBER: 2002166586 EMBASE
TITLE: The products of the UL10 (gM) and the UL49.5 genes of Marek's disease virus serotype 1 are essential for virus growth in cultured cells.
AUTHOR: Tischer B.K.; Schumacher D.; **Messerle M.**; Wagner M.; Osterrieder N.
CORPORATE SOURCE: N. Osterrieder, Institute of Molecular Biology, Friedrich-Loeffler-Institutes, Fed. Res. Ctr. Virus Dis. Animals, Boddenblick 5a, D-17498 Insel Riems, Germany. klaus.osterrieder@rie.bfav.de
SOURCE: Journal of General Virology, (2002) 83/5 (997-1003). Refs: 44
ISSN: 0022-1317 CODEN: JGVIAY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The role of the products of the UL10 and the UL49.5 homologous genes of Marek's disease virus serotype 1 (MDV-1) in virus replication was investigated. Deletion of either open reading frame in an **infectious bacterial artificial chromosome** clone (BAC20) of MDV-1 resulted in progeny viruses that were unable to spread from cell to cell. After transfection of UL10- or UL49.5-negative BAC20 DNA into chicken or quail cells, only single infected cells were observed by indirect immunofluorescence analysis. In contrast, plaque formation was restored when mutant BAC DNAs were co-transfected with the corresponding expression plasmid encoding either the UL10-encoded gM or the UL49.5 gene product. These data demonstrate that gM and its putative complex partner, the UL49.5 homologous protein, are essential for MDV-1 growth in cultured cells. Thus, MDV-1 represents

the first example of a member of the family **Herpesviridae** for which the highly conserved membrane proteins are indispensable for cell-to-cell spread.

L16 ANSWER 12 OF 24 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 7

ACCESSION NUMBER: 2002251388 EMBASE
TITLE: Herpesvirus genetics has come of age.
AUTHOR: Wagner M.; Ruzsics Z.; **Koszinowski U.H.**
CORPORATE SOURCE: M. Wagner, Max von Pettenkofer Institute, Gene Center, Ludwig-Maximilians-University, 81377 Munich, Germany. koszinowski@m3401.mpk.med.uni-muenchen.de
SOURCE: Trends in Microbiology, (1 Jul 2002) 10/7 (318-324). Refs: 67
ISSN: 0966-842X CODEN: TRMIEA
PUBLISHER IDENT.: S 0966-842X(02)02394-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The genetic analysis of the large and complex **herpesviruses** has been a constant challenge to **herpesvirologists**. Elegant methods have been developed to produce mutants in infected cells that rely on the cellular recombination machinery. Bacterial artificial chromosomes (BACs), single copy F-factor-based plasmid vectors of intermediate insert capacity, have now enabled the cloning of **complete herpesvirus** genomes. **Infectious** virus genomes can be shuttled between Escherichia coli and eukaryotic cells. **Herpesvirus** BAC DNA engineering in E. coli by homologous recombination requires neither restriction sites nor cloning steps and allows the introduction of a wide variety of DNA modifications. Such E. coli-based technology has provided a safe, fast and effective approach to the systematic mining of the information stored in **herpesvirus** genomes as a result of their intimate co-evolution with their specific hosts for millions of years. Use of this technique could lead to new developments in clinical virology and basic virology research, and increase the usage of viral genomes as investigative tools and vectors.

L16 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:795048 CAPLUS
DOCUMENT NUMBER: 135:340201
TITLE: Eukaryote cell transformation using cytomegalovirus-based **bacterial artificial chromosome** vector system
INVENTOR(S): Wagner, Markus; **Brune, Wolfram**
PATENT ASSIGNEE(S): Koszinowski, Ulrich H., Germany
SOURCE: Ger. Offen., 36 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10020500	A1	20011031	DE 2000-10020500	20000426
EP 1167529	A2	20020102	EP 2001-109460	20010424
EP 1167529	A3	20020508		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: DE 2000-10020500 A 20000426

AB A vector system for introducing DNA into Eukaryote cells was developed.

This vector system uses bacteria that are found in Eukaryotic cells, or invasive bacteria that are able to penetrate actively. These bacteria are used for construction of bacterial artificial chromosomes (BAC), carrying heterologous DNA. This heterologous DNA contained also viral DNA. The viral DNA can contain addnl. heterologous genes. Depending on the nature of the heterologous genes and on the nature of the viral DNA the vector system can be used for therapy as a vaccine or drug.

L16 ANSWER 14 OF 24 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001111662 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11152518
TITLE: Genetic evidence of an essential role for cytomegalovirus small capsid protein in viral growth.
AUTHOR: Borst E M; Mathys S; Wagner M; Muranyi W; **Messerle M**
CORPORATE SOURCE: Max von Pettenkofer-Institut fur Hygiene und Medizinische Mikrobiologie, Lehrstuhl Virologie, Genzentrum, Ludwig-Maximilians-Universitat Munchen, D-81377 Munich, Germany.
SOURCE: Journal of virology, (2001 Feb) 75 (3) 1450-8. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010202

AB Many steps in the replication cycle of cytomegalovirus (CMV), like cell entry, capsid assembly, and egress of newly synthesized virions, have not been completely analyzed yet. In order to facilitate these studies, we decided to construct a recombinant CMV that incorporates the green fluorescent protein (GFP) into the nucleocapsid. A comparable herpes simplex virus type 1 (HSV-1) mutant has recently been generated by fusion of the GFP open reading frame (ORF) with the HSV-1 ORF encoding small capsid protein (SCP) VP26 (P. Desai and S. Person, J. Virol. 72:7563-7568, 1998). Recombinant CMV genomes expressing a fusion protein consisting of GFP and the SCP were constructed by the recently established **bacterial artificial chromosome** mutagenesis procedure. In transfected cells, the SCP-GFP fusion protein localized to distinct foci in the nucleus that may represent sites for capsid assembly (assemblons). However, no viable progeny was reconstituted from these mutant CMV genomes. **CMV** genomes with deletion of the SCP ORF also did not give rise to **infectious** virus. Rescue of the mutation by insertion of the SCP gene at an ectopic position in an SCP knockout **genome** indicates that, in contrast to the **HSV** -1 SCP, the **CMV** SCP is essential for viral growth. Expression of the SCP-GFP fusion protein together with the authentic SCP blocked the CMV infection cycle, suggesting that the SCP-GFP fusion protein exerts a dominant-negative effect on the assembly of new virions. The results of this study are discussed with regard to recently published data about the structure of the CMV virion and its differences from the HSV-1 virion.

L16 ANSWER 15 OF 24 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2000429895 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10933677
TITLE: Fast screening procedures for random transposon libraries of cloned herpesvirus genomes: mutational analysis of human cytomegalovirus envelope glycoprotein genes.
AUTHOR: Hobom U; **Brune W; Messerle M; Hahn G; Koszinowski U H**
CORPORATE SOURCE: Lehrstuhl fur Virologie, Max von Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, 80336 Munich,

Germany.
SOURCE: Journal of virology, (2000 Sep) 74 (17) 7720-9.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914

AB We have cloned the human **cytomegalovirus** (HCMV) **genome** as an **infectious bacterial artificial chromosome** (BAC) in Escherichia coli. Here, we have subjected the HCMV BAC to random transposon (Tn) mutagenesis using a Tn1721-derived insertion sequence and have provided the conditions for excision of the BAC cassette. We report on a fast and efficient screening procedure for a Tn insertion library. Bacterial clones containing randomly mutated full-length HCMV genomes were transferred into 96-well microtiter plates. A PCR screening method based on two Tn primers and one primer specific for the desired genomic position of the Tn insertion was established. Within three consecutive rounds of PCR a Tn insertion of interest can be assigned to a specific bacterial clone. We applied this method to retrieve mutants of HCMV envelope glycoprotein genes. To determine the infectivities of the mutant HCMV genomes, the DNA of the identified BACs was transfected into permissive fibroblasts. In contrast to BACs with mutations in the genes coding for gB, gH, gL, and gM, which did not yield infectious virus, BACs with disruptions of open reading frame UL4 (gp48) or UL74 (gO) were viable, although gO-deficient viruses showed a severe growth deficit. Thus, gO (UL74), a component of the glycoprotein complex III, is dispensable for viral growth. We conclude that our approach of PCR screening for Tn insertions will greatly facilitate the functional analysis of herpesvirus genomes.

L16 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:494566 CAPLUS
DOCUMENT NUMBER: 133:359596
TITLE: Cloning and mutagenesis of the murine gammaherpesvirus 68 genome as an infectious **bacterial artificial chromosome**
AUTHOR(S): Adler, Heiko; **Messerle, Martin**; Wagner, Markus; **Koszinowski, Ulrich H.**
CORPORATE SOURCE: Max von Pettenkofer-Institut fur Hygiene und Medizinische Mikrobiologie, Lehrstuhl Virologie, Genzentrum, Ludwig-Maximilians-Universitat Munchen, Munich, D-81377, Germany
SOURCE: Journal of Virology (2000), 74(15), 6964-6974
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Gammaherpesviruses cause important infections of humans, in particular in immunocompromised patients. Recently, murine gammaherpesvirus 68 (MHV-68) infection of mice has been developed as a small animal model of gammaherpesvirus pathogenesis. Efficient generation of mutants of MHV-68 would significantly contribute to the understanding of viral gene functions in virus-host interaction, thereby further enhancing the potential of this model. To this end, we cloned the MHV-68 genome as a **bacterial artificial chromosome** (BAC) in Escherichia coli. During propagation in E. coli, spontaneous recombination events within the internal and terminal repeats of the cloned MHV-68 genome, affecting the copy number of the repeats, were occasionally observed The gene for the green fluorescent protein was incorporated into the cloned BAC for identification of infected cells.

BAC vector sequences were flanked by loxP sites to allow the excision of these sequences using recombinase Cre and to allow the generation of recombinant viruses with wild-type genome properties. Infectious virus was reconstituted from the BAC-cloned MHV-68. Growth of the BAC-derived virus in cell culture was indistinguishable from that of wild-type MHV-68. To assess the feasibility of mutagenesis of the cloned MHV-68 genome, a mutant virus with a deletion of open reading frame 4 was generated. Genetically modified MHV-68 can now be analyzed in functionally modified mouse strains to assess the role of gammaherpesvirus genes in virus-host interaction and pathogenesis.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 24 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2000148976 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10684299
TITLE: Identification of a boundary domain adjacent to the potent human cytomegalovirus enhancer that represses transcription of the divergent UL127 promoter.
AUTHOR: Angulo A; Kerry D; Huang H; Borst E M; Razinsky A; Wu J; Hobom U; **Messerle M**; Ghazal P
CORPORATE SOURCE: Department of Immunology and Molecular Biology, Division of Virology, The Scripps Research Institute, La Jolla, California 92037, USA.
SOURCE: Journal of virology, (2000 Mar) 74 (6) 2826-39. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000413
Last Updated on STN: 20000413
Entered Medline: 20000403

AB Transcriptional repression within a complex modular promoter may play a key role in determining the action of enhancer elements. In human cytomegalovirus, the major immediate-early promoter (MIEP) locus contains a highly potent and complex modular enhancer. Evidence is presented suggesting that sequences of the MIEP between nucleotide positions -556 and -673 function to prevent transcription activation by enhancer elements from the UL127 open reading frame divergent promoter. Transient transfection assays of reporter plasmids revealed repressor sequences located between nucleotides -556 and -638. The ability of these sequences to confer repression in the context of an infection was shown using recombinant viruses generated from a **bacterial artificial chromosome** containing an **infectious** human **cytomegalovirus genome**. In addition to repressor sequences between -556 and -638, infection experiments using recombinant virus mutants indicated that sequences between -638 and -673 also contribute to repression of the UL127 promoter. On the basis of in vitro transcription and transient transfection assays, we further show that interposed viral repressor sequences completely inhibit enhancer-mediated activation of not only the homologous but also heterologous promoters. These and other experiments suggest that repression involves an interaction of host-encoded regulatory factors with defined promoter sequences that have the property of proximally interfering with upstream enhancer elements in a chromatin-independent manner. Altogether, our findings establish the presence of a boundary domain that efficiently blocks enhancer-promoter interactions, thus explaining how the enhancer can work to selectively activate the MIEP.

L16 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:849927 CAPLUS
DOCUMENT NUMBER: 135:163005

TITLE: Cytomegalovirus bacterial artificial chromosomes: a new herpesvirus vector approach
AUTHOR(S): **Messerle, Martin; Hahn, Gabriele; Brune, Wolfram; Koszinowski, Ulrich H.**
CORPORATE SOURCE: Department of Virology Max von Pettenkofer Institute for Hygiene and Medical Microbiology, Ludwig-Maximilians-University of Munich, Munich, 80336, Germany
SOURCE: Advances in Virus Research (2000), 55, 463-478
CODEN: AVREA8; ISSN: 0065-3527
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 76 refs. Topics include: feature of **CMV** that qualify it as a vector (cloning capacity, **CMV** immune evasion genes, cell tropism), manipulation of **CMV genome**, and engineering of **CMV** vectors for gene transfer (investigating cloning capacity, construction of replication-deficient vectors, promoters for transgene expression, **CMV** amplicon vectors). (c) 2000 Academic Press.
REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 19 OF 24 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 11
ACCESSION NUMBER: 2000:387696 BIOSIS
DOCUMENT NUMBER: PREV200000387696
TITLE: Forward with BACs: New tools for herpesvirus genomics.
AUTHOR(S): **Brune, Wolfram** [Reprint author]; **Messerle, Martin** [Reprint author]; **Koszinowski, Ulrich H.** [Reprint author]
CORPORATE SOURCE: Max von Pettenkofer Institute, Department of Virology, University of Munich, Munich, Germany
SOURCE: Trends in Genetics, (June, 2000) Vol. 16, No. 6, pp. 254-259. print.
CODEN: TRGEE2. ISSN: 0168-9525.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2000
Last Updated on STN: 8 Jan 2002

L16 ANSWER 20 OF 24 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2001051539 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10933196
TITLE: Development of a cytomegalovirus vector for somatic gene therapy.
AUTHOR: Borst E; **Messerle M**
CORPORATE SOURCE: Max von Pettenkofer-Institut, Abteilung Virologie, Genzentrum, Ludwig-Maximilians-Universitat Munchen, Germany.
SOURCE: Bone marrow transplantation, (2000 May) 25 Suppl 2 S80-2.
Journal code: 8702459. ISSN: 0268-3369.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001212
AB The development of new and improved vector systems is central for realization of new concepts for gene therapy. The tropism of human **cytomegalovirus** (**CMV**) for hematopoietic progenitor cells and the large **genome** size (230 kbp) that offers a unique cloning

capacity make this virus a promising vector candidate for gene transfer into hematopoietic cells and for therapy of congenital and acquired diseases of the hematopoietic system. Recently, we cloned the **CMV genome** as a **bacterial artificial chromosome** (BAC) in Escherichia coli and established efficient mutagenesis procedures for **CMV** - a prerequisite for vector construction. Here, we report on the construction of a recombinant GFP virus that will be used to re-evaluate the tropism of CMV and to monitor gene transfer into target cells. Further goals of CMV vector development are the evaluation of the cloning capacity and the construction of replication-deficient vectors.

L16 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:101304 CAPLUS
DOCUMENT NUMBER: 130:163960
TITLE: Cloning intact, infectious large virus genomes using bacterial artificial chromosomes and in vivo recombination to create a circular minichromosome
INVENTOR(S): **Koszinowski, Ulrich; Messerle, Martin**
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19733364	A1	19990204	DE 1997-19733364	19970801
WO 9906582	A1	19990211	WO 1998-EP4816	19980731
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9893385	A1	19990222	AU 1998-93385	19980731
EP 996738	A1	20000503	EP 1998-946268	19980731
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, IE				

PRIORITY APPLN. INFO.: DE 1997-19733364 A 19970801
WO 1998-EP4816 W 19980731

AB A method of cloning essentially **complete**, intact, replication-competent and **infectious** genomes from virus with very large genomes such as the **cytomegaloviruses** is described. The method involves using in vivo recombination of a **bacterial artificial chromosome** and the virus in an animal cell with the formation of a circular minichromosome that can be isolated, propagated in a **bacterial** host, and manipulated. The vector carries a fragment of the target virus genome to create a site for homologous recombination. Use of in vivo recombination in Escherichia coli to inactivate mouse cytomegalovirus immediate-early gene 1 is demonstrated.

L16 ANSWER 22 OF 24 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1999412347 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10482582
TITLE: Cloning of the human **cytomegalovirus** (HCMV) **genome** as an **infectious bacterial artificial chromosome** in Escherichia coli: a new approach for construction of HCMV mutants.
AUTHOR: Borst E M; **Hahn G; Koszinowski U H; Messerle M**
CORPORATE SOURCE: Max von Pettenkofer-Institut fur Hygiene und Medizinische Mikrobiologie, Ludwig-Maximilians-Universitat Munchen, D-81377 Munich, Germany.

SOURCE: Journal of virology, (1999 Oct) 73 (10) 8320-9.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991012

AB We have recently introduced a novel procedure for the construction of **herpesvirus** mutants that is based on the cloning and mutagenesis of **herpesvirus** genomes as **infectious** bacterial artificial chromosomes (BACs) in Escherichia coli (M. Messerle, I. Crnkovic, W. Hammerschmidt, H. Ziegler, and U. H. Koszinowski, Proc. Natl. Acad. Sci. USA 94:14759-14763, 1997). Here we describe the application of this technique to the human cytomegalovirus (HCMV) strain AD169. Since it was not clear whether the terminal and internal repeat sequences of the HCMV genome would give rise to recombination, the stability of the cloned HCMV genome was examined during propagation in E. coli, during mutagenesis, and after transfection in permissive fibroblasts. Interestingly, the HCMV BACs were frozen in defined conformations in E. coli. The transfection of the HCMV BACs into human fibroblasts resulted in the reconstitution of infectious virus and isomerization of the reconstituted genomes. The power of the BAC mutagenesis procedure was exemplarily demonstrated by the disruption of the gpUL37 open reading frame. The transfection of the mutated BAC led to plaque formation, indicating that the gpUL37 gene product is dispensable for growth of HCMV in fibroblasts. The new procedure will considerably speed up the construction of HCMV mutants and facilitate genetic analysis of HCMV functions.

L16 ANSWER 23 OF 24 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 1999329236 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10400809
TITLE: Systematic excision of vector sequences from the BAC-cloned **herpesvirus genome** during virus reconstitution.
AUTHOR: Wagner M; Jonjic S; **Koszinowski U H**; **Messerle M**
CORPORATE SOURCE: Max von Pettenkofer-Institut fur Hygiene und Medizinische Mikrobiologie, Ludwig-Maximilians-Universitat Munchen, D-81377 Munich, Germany.
SOURCE: Journal of virology, (1999 Aug) 73 (8) 7056-60.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
Entered Medline: 19990824

AB Recently the mouse **cytomegalovirus** (MCMV) **genome** was cloned as an **infectious bacterial artificial chromosome** (BAC) (M. Messerle, I. Crnkovic, W. Hammerschmidt, H. Ziegler, and U. H. Koszinowski, Proc. Natl. Acad. Sci. USA 94:14759-14763, 1997). The virus obtained from this construct is attenuated in vivo due to deletion of viral sequences and insertion of the BAC vector. We reconstituted the full-length MCMV genome and flanked the BAC vector with identical viral sequences. This new construct represents a versatile basis for construction of MCMV mutants since virus generated from the construct loses the bacterial sequences and acquires wild-type properties.

L16 ANSWER 24 OF 24 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1998070825 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9405686
TITLE: Cloning and mutagenesis of a **herpesvirus genome** as an **infectious bacterial artificial chromosome**.
AUTHOR: **Messerle M**; Crnkovic I; Hammerschmidt W; Ziegler H; **Koszinowski U H**
CORPORATE SOURCE: Max von Pettenkofer-Institut fur Hygiene und Mikrobiologie, Ludwig-Maximilians-Universitat Munchen, Feodor-Lynen-Strasse 25, D-81377 Munich, Germany.. Messerle@lmb.uni-muenchen.de
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Dec 23) 94 (26) 14759-63. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19980217
Entered Medline: 19980202

AB A strategy for cloning and mutagenesis of an **infectious herpesvirus genome** is described. The mouse **cytomegalovirus genome** was cloned and maintained as a 230 kb **bacterial artificial chromosome** (BAC) in E. coli. Transfection of the BAC plasmid into eukaryotic cells led to a productive virus infection. The feasibility to introduce targeted mutations into the BAC cloned virus genome was shown by mutation of the immediate-early 1 gene and generation of a mutant virus. Thus, the **complete** construction of a mutant **herpesvirus genome** can now be carried out in a controlled manner prior to the reconstitution of **infectious** progeny. The described approach should be generally applicable to the mutagenesis of genomes of other large DNA viruses.

=> D HIS

(FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
L1 802 S (KOSZINOWSKI, ?)/IN,AU
L2 537 S (MESSERLE, ?)/IN,AU
L3 5359 S (BRUNE, ?)/IN,AU
L4 43708 S (HAHN, ?)/IN,AU
L5 7 S L1 AND L2 AND L3 AND L4
L6 3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7 50178 S L1 OR L2 OR L3 OR L4
L8 5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9 16997 S BAC OR L8
L10 381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11 387 S L8 AND L10
L12 82 S L11 AND L7
L13 27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14 207 S L13 AND L8
L15 60 S L14 AND L7
L16 24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)

=> S L12 NOT L15
L17 22 L12 NOT L15

=> DUPLICATE REMOVE L17
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N
PROCESSING COMPLETED FOR L17
L18 12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)

=> D IBIB AB L18 1-12

L18 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:473225 CAPLUS
DOCUMENT NUMBER: 141:34688
TITLE: Novel virus encoded chemokines determine the tissue tropism of human **cytomegalovirus** (HCMV)
INVENTOR(S): **Hahn, Gabriele**
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 56 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004110188	A1	20040610	US 2003-619189	20030715
DE 10232322	A1	20040729	DE 2002-10232322	20020716
PRIORITY APPLN. INFO.:			DE 2002-10232322 A	20020716

AB The present invention relates to the UL131-128 transcripts of clin. isolates of HCMV. The genetic determinants of endothelial cell and leukocyte tropism were assigned to the UL132-UL128 genetic locus of HCMV. Translation of the newly identified transcripts showed novel open reading frames (orfs) coding for novel putative C+C and CC chemokines which are of crucial importance for HCMV pathogenesis and tissue tropism. The invention also relates to the study and synthesis of the newly disclosed protein products HCK-1, HCK-2, HCK-3, HCK-4 and HCK-5 as well as other potential proteins encoded by the UL132-UL128 and UL131-128 genetic region.

L18 ANSWER 2 OF 12 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004083840 EMBASE
TITLE: Expansion of Protective CD8(+) T-Cell Responses Driven by Recombinant **Cytomegaloviruses**.
AUTHOR: Karrer U.; Wagner M.; Sierro S.; Oxenius A.; Hengel H.; Dumrese T.; Freigang S.; **Koszinowski U.H.**; Phillips R.E.; Klenerman P.
CORPORATE SOURCE: U. Karrer, Department of Medicine, Division of Infectious Diseases, University Hospital of Zurich, Ramistrasse 100, 8091 Zurich, United Kingdom. urs.karrer@usz.ch
SOURCE: Journal of Virology, (2004) 78/5 (2255-2264).
Refs: 63
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB CD8(+) T cells are critical for the control of many persistent viral infections, such as human immunodeficiency virus, hepatitis C virus, Epstein-Barr virus, and **cytomegalovirus** (**CMV**). In most infections, large CD8(+)-T-cell populations are induced early but then contract and are maintained thereafter at lower levels. In contrast, CD8(+) T cells specific for murine **CMV** (MCMV) have been shown to

gradually accumulate after resolution of primary infection. This unique behavior is restricted to certain epitopes, including an immunodominant epitope derived from the immediate-early 1 (IE1) gene product. To explore the mechanism behind this further, we measured CD8(+)-T-cell-mediated immunity induced by recombinant MCMV-expressing epitopes derived from influenza A virus or lymphocytic choriomeningitis virus placed under the control of an IE promoter. We observed that virus-specific CD8(+)-T-cell populations were induced and that these expanded gradually over time. Importantly, these CD8(+) T cells provided long-term protection against challenge without boosting. These results demonstrate a unique pattern of accumulating T cells, which provide long-lasting immune protection, that is independent of the initial immunodominance of the epitope and indicates the potential of T-cell-inducing vaccines based on persistent vectors.

L18 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:360967 CAPLUS
DOCUMENT NUMBER: 141:34312
TITLE: Mutagenesis of **herpesvirus** BACs by allele replacement
AUTHOR(S): Borst, Eva-Maria; Posfai, Gyorgy; Pogoda, Frank; **Messerle, Martin**
CORPORATE SOURCE: Virus Cell Interaction Unit, Medical Faculty, Martin-Luther Universitaet, Halle, Germany
SOURCE: Methods in Molecular Biology (Totowa, NJ, United States) (2004), 256(Bacterial Artificial Chromosomes, Volume 2), 269-279
CODEN: MMBIED; ISSN: 1064-3745
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A two-step replacement procedure is highly useful for mutagenesis of **bacterial artificial chromosome** (BAC)-cloned **herpesvirus** genomes. The method involves transformation of the shuttle plasmid carrying the desired mutation plus flanking homologies (A and B) into bacteria that already contain BAC, and through homologous recombination via region A or B the shuttle plasmid is completely integrated into the viral BAC genome, leading to cointegrate. A mutagenesis procedure using the two-step replacement method for using a shuttle plasmid that is based on the vector pST76-KSR encoding kanamycin resistance is described.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2003:184927 BIOSIS
DOCUMENT NUMBER: PREV200300184927
TITLE: Cloning of **herpesviral** genomes as bacterial artificial chromosomes.
AUTHOR(S): Adler, Heiko [Reprint Author]; **Messerle, Martin**; **Koszinowski, Ulrich H.**
CORPORATE SOURCE: Clinical Cooperation Group Hematopoietic Cell Transplantation, GSF-Research Center for Environment and Health, Institute of Molecular Immunology, Marchioninistrasse 25, D-81377, Munich, Germany
h.adler@gsf.de
SOURCE: Reviews in Medical Virology, (Mar-Apr 2003) Vol. 13, No. 2, pp. 111-121. print.
ISSN: 1052-9276 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Apr 2003
Last Updated on STN: 9 Apr 2003

L18 ANSWER 5 OF 12 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002430514 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12186938
TITLE: The human **cytomegalovirus** ribonucleotide reductase homolog UL45 is dispensable for growth in endothelial cells, as determined by a BAC-cloned clinical isolate of human **cytomegalovirus** with preserved wild-type characteristics.
AUTHOR: **Hahn Gabriele**; Khan Hanna; Baldanti Fausto; **Koszinowski Ulrich H**; Revello M Grazia; Gerna Giuseppe
CORPORATE SOURCE: Max von Pettenkofer Institut fur Virologie, Ludwig-Maximilians-Universitat Munchen, 80336 Munich, Germany.. ghahn@m3401.mpk.med.uni-muenchen.de
SOURCE: Journal of virology, (2002 Sep) 76 (18) 9551-5. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020821
Last Updated on STN: 20021003
Entered Medline: 20021002

AB An endothelial cell-tropic and leukotropic human **cytomegalovirus** (HCMV) clinical isolate was cloned as a fusion-inducing factor X-**bacterial artificial chromosome** in Escherichia coli, and the ribonucleotide reductase homolog UL45 was deleted. Reconstituted virus RVFIX and RV Delta UL45 grew equally well in human fibroblasts and human endothelial cells. Thus, UL45 is dispensable for growth of HCMV in both cell types.

L18 ANSWER 6 OF 12 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002294950 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11961253
TITLE: The products of the UL10 (gM) and the UL49.5 genes of Marek's disease virus serotype 1 are essential for virus growth in cultured cells.
AUTHOR: Tischer B Karsten; Schumacher Daniel; **Messerle Martin**; Wagner Markus; Osterrieder Nikolaus
CORPORATE SOURCE: Institute of Molecular Biology, Friedrich-Loeffler-Institutes, Federal Research Centre for Virus Diseases of Animals, Boddenblick 5a, D-17498 Insel Riems, Germany.
SOURCE: Journal of general virology, (2002 May) 83 (Pt 5) 997-1003. Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020531
Last Updated on STN: 20020613
Entered Medline: 20020612

AB The role of the products of the UL10 and the UL49.5 homologous genes of Marek's disease virus serotype 1 (MDV-1) in virus replication was investigated. Deletion of either open reading frame in an infectious **bacterial artificial chromosome** clone (BAC20) of MDV-1 resulted in progeny viruses that were unable to spread from cell to cell. After transfection of UL10- or UL49.5-negative BAC20 DNA into chicken or quail cells, only single infected cells were observed by indirect immunofluorescence analysis. In contrast, plaque formation was restored when mutant BAC DNAs were co-transfected with the corresponding expression plasmid encoding either the UL10-encoded gM or the UL49.5 gene

product. These data demonstrate that gM and its putative complex partner, the UL49.5 homologous protein, are essential for MDV-1 growth in cultured cells. Thus, MDV-1 represents the first example of a member of the family **Herpesviridae** for which the highly conserved membrane proteins are indispensable for cell-to-cell spread.

L18 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001264747 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11356978
TITLE: Virus reconstituted from infectious **bacterial artificial chromosome** (BAC)-cloned murine gammaherpesvirus 68 acquires wild-type properties in vivo only after excision of BAC vector sequences.
AUTHOR: Adler H; **Messerle M; Koszinowski U H**
CORPORATE SOURCE: Max von Pettenkofer-Institut fur Hygiene und Medizinische Mikrobiologie, Lehrstuhl Virologie, Genzentrum, Ludwig-Maximilians-Universitat Munchen, D-81377 Munich, Germany.. adler@lmb.uni-muenchen.de
SOURCE: Journal of virology, (2001 Jun) 75 (12) 5692-6.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621

AB We studied the in vivo biological properties of viruses reconstituted from the genome of murine gammaherpesvirus 68 (MHV-68) cloned as an infectious **bacterial artificial chromosome** (BAC). Recombinant virus RgammaHV68A98.01, containing BAC vector sequences, is attenuated in vivo as determined by (i) viral titers in the lungs during the acute phase of infection, (ii) the extent of splenomegaly, and (iii) the number of latently infected spleen cells reactivating virus in an ex vivo reactivation assay. Since the BAC vector sequences were flanked by loxP sites, passaging the virus in fibroblasts expressing Cre recombinase resulted in the generation of recombinant virus RgammaHV68A98.02, with biological properties comparable to those of wild-type MHV-68. On the basis of these data we conclude (i) that excision of BAC vector sequences from cloned MHV-68 genomes is critical for reconstitution of the wild-type phenotypic properties of this virus and (ii) that the BAC-cloned MHV-68 genome is suitable for the construction of mutants and mutant libraries whose phenotypes can be reliably assessed in vivo.

L18 ANSWER 8 OF 12 BIOSIS on STN
ACCESSION NUMBER: 2002:253098 BIOSIS
DOCUMENT NUMBER: PREV200200253098
TITLE: **Cytomegalovirus** bacterial artificial chromosomes: A new **herpesvirus** vector approach.
AUTHOR(S): **Messerle, Martin** [Reprint author]; **Hahn, Gabriele** [Reprint author]; **Brune, Wolfram** [Reprint author]; **Koszinowski, Ulrich H.** [Reprint author]
CORPORATE SOURCE: Max von Pettenkofer Institute for Hygiene and Medical Microbiology, Ludwig-Maximilians-Univeristy of Munich, Pettenkofer-Strasse 9a, 80336, Munich, Germany
SOURCE: Maramorosch, Karl [Editor]; Murphy, Frederick A. [Editor]; Shatkin, Aaron J. [Editor]. Adv. Virus Res., (2000) pp. 463-478. Advances in Virus Research. print.
Publisher: Academic Press Inc., 525 B Street, Suite 1900, San Diego, CA, 92101-4495, USA; Academic Press Ltd., 24-28

Oval Road, London, NW1 7DX, UK. Series: Advances in Virus Research.
CODEN: AVREA8. ISSN: 0065-3527. ISBN: 0-12-039855-9 (cloth).
DOCUMENT TYPE: Book
Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002

L18 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001046581 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11070009
TITLE: The major immediate-early gene ie3 of mouse **cytomegalovirus** is essential for viral growth.
AUTHOR: Angulo A; Ghazal P; **Messerle M**
CORPORATE SOURCE: Department of Immunology and Molecular Biology, Division of Virology, The Scripps Research Institute, La Jolla, California 92037, USA.. angulo@scripps.edu
CONTRACT NUMBER: AI-30627 (NIAID)
SOURCE: Journal of virology, (2000 Dec) 74 (23) 11129-36.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001204

AB The significance of the major immediate-early gene ie3 of mouse **cytomegalovirus** (MCMV) and that of the corresponding ie2 gene of human **cytomegalovirus** to viral replication are not known. To investigate the function of the MCMV IE3 regulatory protein, we generated two different MCMV recombinants that contained a large deletion in the IE3 open reading frame (ORF). The mutant genomes were constructed by the **bacterial artificial chromosome** mutagenesis technique, and MCMV ie3 deletion mutants were reconstituted on a mouse fibroblast cell line that expresses the MCMV major immediate-early genes. The ie3 deletion mutants failed to replicate on normal mouse fibroblasts even when a high multiplicity of infection was used. The replication defect was rescued when the IE3 protein was provided in trans by a complementing cell line. A revertant virus in which the IE3 ORF was restored was able to replicate with wild-type kinetics in normal mouse fibroblasts, providing evidence that the defective growth phenotype of the ie3 mutants was due to disruption of the ie3 gene. To characterize the point of restriction in viral replication that is controlled by ie3, we analyzed the pattern of expression of selective early (beta) and late (gamma) genes. While we could detect transcripts for the immediate-early gene ie1 in cells infected with the ie3 mutants, we failed to detect transcripts for representative beta and gamma genes. These data demonstrate that the MCMV transactivator IE3 plays an indispensable role during viral replication in tissue culture, implicating a similar role for the human **CMV** ie2 gene product. To our knowledge, the ie3 deletion mutants represent the first MCMV recombinants isolated that contain a disruption of an essential gene.

L18 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:347046 BIOSIS
DOCUMENT NUMBER: PREV200000347046
TITLE: Cloning and mutagenesis of the murine gammaherpesvirus 68 genome as an infectious **bacterial artificial chromosome**.

AUTHOR(S): Adler, Heiko; **Messerle, Martin**; Wagner, Markus; **Koszinowski, Ulrich H.** [Reprint author]
CORPORATE SOURCE: Lehrstuhl Virologie, Max von Pettenkofer-Institut fuer Hygiene und Medizinische Mikrobiologie, Ludwig-Maximilians-Universitaet Muenchen, Pettenkofer-Strasse 9a, D-80336, Munich, Germany
SOURCE: Journal of Virology, (August, 2000) Vol. 74, No. 15, pp. 6964-6974. print.
CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Aug 2000
Last Updated on STN: 7 Jan 2002

AB Gammaherpesviruses cause important infections of humans, in particular in immunocompromised patients. Recently, murine gammaherpesvirus 68 (MHV-68) infection of mice has been developed as a small animal model of gammaherpesvirus pathogenesis. Efficient generation of mutants of MHV-68 would significantly contribute to the understanding of viral gene functions in virus-host interaction, thereby further enhancing the potential of this model. To this end, we cloned the MHV-68 genome as a **bacterial artificial chromosome** (BAC) in Escherichia coli. During propagation in E. coli, spontaneous recombination events within the internal and terminal repeats of the cloned MHV-68 genome, affecting the copy number of the repeats, were occasionally observed. The gene for the green fluorescent protein was incorporated into the cloned BAC for identification of infected cells. BAC vector sequences were flanked by loxP sites to allow the excision of these sequences using recombinase Cre and to allow the generation of recombinant viruses with wild-type genome properties. Infectious virus was reconstituted from the BAC-cloned MHV-68. Growth of the BAC-derived virus in cell culture was indistinguishable from that of wild-type MHV-68. To assess the feasibility of mutagenesis of the cloned MHV-68 genome, a mutant virus with a deletion of open reading frame 4 was generated. Genetically modified MHV-68 can now be analyzed in functionally modified mouse strains to assess the role of gammaherpesvirus genes in virus-host interaction and pathogenesis.

L18 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2000287748 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10827452
TITLE: Forward with BACs: new tools for **herpesvirus** genomics.
AUTHOR: **Brune W; Messerle M; Koszinowski U H**
CORPORATE SOURCE: Max von Pettenkofer Institute, Department of Virology, University of Munich, Germany.. wolfram@lmb.uni-muenchen.de
SOURCE: Trends in genetics : TIG, (2000 Jun) 16 (6) 254-9. Ref: 39
Journal code: 8507085. ISSN: 0168-9525.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000719

AB The large, complex genomes of **herpesviruses** document the high degree of adaptation of these viruses to their hosts. Not surprisingly, the methods developed over the past 30 years to analyse **herpesvirus** genomes have paralleled those used to investigate the genetics of eukaryotic cells. The recent use of **bacterial artificial chromosome** (BAC) technology in

herpesvirus genetics has made their genomes accessible to the tools of **bacterial** genetics. This has opened up new avenues for reverse and forward genetics of this virus family in basic research, and also for vector and vaccine development.

L18 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2000:369826 BIOSIS
DOCUMENT NUMBER: PREV200000369826
TITLE: Development of a **cytomegalovirus** vector for somatic gene therapy.
AUTHOR(S): Borst, E.; **Messerle, M.** [Reprint author]
CORPORATE SOURCE: Genzentrum, Max von Pettenkofer-Institut, Ludwig-Maximilians-Universitaet Muenchen, Feodor-Lynen-Strasse 25, D-81377, Muenchen, Germany
SOURCE: Bone Marrow Transplantation, (May, 2000) Vol. 25, No. Supplement 2, pp. S80-S82. print.
Meeting Info.: 2nd International Symposium on Transplantation and Gene Therapy. Idar-Oberstein, Germany. October 21-23, 1999.
ISSN: 0268-3369.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Paper)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 2000
Last Updated on STN: 8 Jan 2002

=> D HIS

(FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
L1 802 S (KOSZINOWSKI, ?)/IN,AU
L2 537 S (MESSERLE, ?)/IN,AU
L3 5359 S (BRUNE, ?)/IN,AU
L4 43708 S (HAHN, ?)/IN,AU
L5 7 S L1 AND L2 AND L3 AND L4
L6 3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7 50178 S L1 OR L2 OR L3 OR L4
L8 5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9 16997 S BAC OR L8
L10 381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11 387 S L8 AND L10
L12 82 S L11 AND L7
L13 27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14 207 S L13 AND L8
L15 60 S L14 AND L7
L16 24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17 22 S L12 NOT L15
L18 12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)

=> S L11 NOT L12
L19 305 L11 NOT L12

=> S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L20 5 (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU

=> DUPLICATE REMOVE L20
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):N
PROCESSING COMPLETED FOR L20

L21 2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)

=> D IBIB AB L21 1,2

L21 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:837254 CAPLUS
DOCUMENT NUMBER: 139:302989
TITLE: VAC-BAC shuttle vector system comprising modified vaccinia virus and use for gene expression
INVENTOR(S): **Moss, Bernard; Domi, Arban**
PATENT ASSIGNEE(S): Government of the United States of America, as Represented by the Secretary Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087330	A2	20031023	WO 2003-US11183	20030410
WO 2003087330	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1495125	A2	20050112	EP 2003-718343	20030410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:		
US 2002-371840P	P	20020410
US 2002-402824P	P	20020809
WO 2003-US11183	W	20030410

AB The invention relates to a VAC-BAC shuttle vector system for creation of recombinant poxviruses from DNA cloned in a bacterial artificial chromosome. The VAC-BAC vector system contains a vaccinia virus genome (VAC) that can replicate in bacteria and produce infectious virus in mammalian cells. The VAC-BAC vector system can be used to modify vaccinia virus DNA by deletion, insertion or point mutation or add new DNA to the VAC genome with methods developed for bacterial plasmids, rather than by recombination in mammalian cells. It can also be used to produce recombinant vaccinia viruses for gene expression and production of modified vaccinia viruses that have improved safety or immunogenicity.

L21 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002475734 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12196634
TITLE: Cloning the vaccinia virus genome as a bacterial artificial chromosome in Escherichia coli and recovery of infectious virus in mammalian cells.
AUTHOR: **Domi Arban; Moss Bernard**
CORPORATE SOURCE: Laboratory of Viral Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892-0445, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2002 Sep 17) 99 (19) 12415-20. Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020919
Last Updated on STN: 20030105
Entered Medline: 20021028

AB The ability to manipulate the vaccinia virus (VAC) genome, as a plasmid in bacteria, would greatly facilitate genetic studies and provide a powerful alternative method of making recombinant viruses. VAC, like other poxviruses, has a linear, double-stranded DNA genome with covalently closed hairpin ends that are resolved from transient head-to-head and tail-to-tail concatemers during replication in the cytoplasm of infected cells. Our strategy to construct a nearly 200,000-bp VAC-bacterial artificial chromosome (BAC) was based on circularization of head-to-tail concatemers of VAC DNA. Cells were infected with a recombinant VAC containing inserted sequences for plasmid replication and maintenance in Escherichia coli; DNA concatemer resolution was inhibited leading to formation and accumulation of head-to-tail concatemers, in addition to the usual head-to-head and tail-to-tail forms; the concatemers were circularized by homologous or Cre-loxP-mediated recombination; and E. coli were transformed with DNA from the infected cell lysates. Stable plasmids containing the entire VAC genome, with an intact concatemer junction sequence, were identified. Rescue of infectious VAC was consistently achieved by transfecting the VAC-BAC plasmids into mammalian cells that were infected with a helper nonreplicating fowlpox virus.

=> D HIS

(FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
L1 802 S (KOSZINOWSKI, ?)/IN,AU
L2 537 S (MESSERLE, ?)/IN,AU
L3 5359 S (BRUNE, ?)/IN,AU
L4 43708 S (HAHN, ?)/IN,AU
L5 7 S L1 AND L2 AND L3 AND L4
L6 3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7 50178 S L1 OR L2 OR L3 OR L4
L8 5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9 16997 S BAC OR L8
L10 381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11 387 S L8 AND L10
L12 82 S L11 AND L7
L13 27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14 207 S L13 AND L8
L15 60 S L14 AND L7
L16 24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17 22 S L12 NOT L15
L18 12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19 305 S L11 NOT L12
L20 5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
L21 2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)

=> S (MOSS, ?)/IN,AU OR (DOMI, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L22 33498 (MOSS, ?)/IN,AU OR (DOMI, ?)/IN,AU

=> S L19 AND L22
L23 0 L19 AND L22

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=> S L9 AND L10
L24         557 L9 AND L10

=> S L24 AND L7
L25          93 L24 AND L7

=> S L25 NOT L12
L26          11 L25 NOT L12

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DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L26
L27            4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)

=> D IBIB AB L27 1-4

L27  ANSWER 1 OF 4  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation.  on STN
ACCESSION NUMBER:   2003:75739  BIOSIS
DOCUMENT NUMBER:    PREV200300075739
TITLE:              Strategies for the identification and analysis of viral
                    immune-evasive genes: Cytomegalovirus as an
                    example.
AUTHOR(S):          Gutermann, A. [Reprint Author]; Bubeck, A. [Reprint
                    Author]; Wagner, M. [Reprint Author]; Reusch, U. [Reprint
                    Author]; Menard, C. [Reprint Author]; Koszinowski, U.
                    H. [Reprint Author]
CORPORATE SOURCE:   Max-von-Pettenkofer Institut, Ludwig-Maximilians-
                    Universitaet Muenchen, 80336, Muenchen, Germany
SOURCE:             Koszinowski, U. H. [Editor, Reprint Author];
                    Hengel, H. [Editor]. (2002) pp. 1-22. Viral proteins
                    counteracting host defenses. print.
                    Publisher: Springer-Verlag New York Inc., 175 Fifth Avenue,
                    New York, NY, 10010-7858, USA; Springer-Verlag GmbH & Co.
                    KG, Heidelberger Platz 3, D-14197, Berlin, Germany. Series:
                    Current Topics in Microbiology and Immunology.
                    ISSN: 0070-217X (ISSN print). ISBN: 3-540-43261-2 (cloth).
DOCUMENT TYPE:      Book; (Book Chapter)
LANGUAGE:           English
ENTRY DATE:         Entered STN: 6 Feb 2003
                    Last Updated on STN: 6 Feb 2003

L27  ANSWER 2 OF 4     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2002051341     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11773401
TITLE:              Proteolytic processing of human cytomegalovirus
                    glycoprotein B is dispensable for viral growth in culture.
AUTHOR:             Strive Tanja; Borst Eva; Messerle Martin; Radsak
                    Klaus
CORPORATE SOURCE:   Institut fur Virologie der Philipps-Universitat, 35037
                    Marburg, Germany.
SOURCE:             Journal of virology, (2002 Feb) 76 (3) 1252-64.
                    Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200202
ENTRY DATE:         Entered STN: 20020125
                    Last Updated on STN: 20020213
                    Entered Medline: 20020212
AB   Glycoprotein B (gB) of human cytomegalovirus (HCMV), which is
     considered essential for the viral life cycle, is proteolytically
     processed during maturation.  Since gB homologues of several other
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herpesviruses remain uncleaved, the relevance of this property of HCMV gB for viral infectivity is unclear. Here we report on the construction of a viral mutant in which the recognition site of gB for the cellular endoprotease furin was destroyed. Because mutagenesis of essential proteins may result in a lethal phenotype, a replication-deficient HCMV gB-null genome encoding enhanced green fluorescent protein was constructed, and complementation by mutant gBs was initially evaluated in transient-cotransfection assays. Cotransfection of plasmids expressing authentic gB or gB with a mutated cleavage site (gB-DeltaFur) led to the formation of green fluorescent miniplaques which were considered to result from one cycle of phenotypic complementation of the gB-null genome. To verify these results, two recombinant HCMV genomes were constructed: HCMV-**BAC**-DeltaMhdI, with a deletion of hydrophobic domain 1 of gB that appeared to be essential for viral growth in the cotransfection experiments, and HCMV-BACDeltaFur, in which the gB cleavage site was mutated by amino acid substitution. Consistent with the results of the cotransfection assays, only the DeltaFur mutant replicated in human fibroblasts, showing growth kinetics comparable to that of wild-type virus. gB in mutant-infected cells was uncleaved, whereas glycosylation and transport to the cell surface were not impaired. Extracellular mutant virus contained exclusively uncleaved gB, indicating that proteolytic processing of gB is dispensable for viral replication in cell culture.

L27 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002364421 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12110210
TITLE: **Herpesvirus** genetics has come of age.
AUTHOR: Wagner Markus; Ruzsics Zsolt; **Koszinowski Ulrich H**
CORPORATE SOURCE: Max von Pettenkofer Institute, Department of Virology, Gene Center, Ludwig-Maximilians-University, 81377 Munich, Germany.
SOURCE: Trends in microbiology, (2002 Jul) 10 (7) 318-24. Ref: 67
Journal code: 9310916. ISSN: 0966-842X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020712
Last Updated on STN: 20020814
Entered Medline: 20020813

AB The genetic analysis of the large and complex **herpesviruses** has been a constant challenge to **herpesvirologists**. Elegant methods have been developed to produce mutants in infected cells that rely on the cellular recombination machinery. Bacterial artificial chromosomes (BACs), single copy F-factor-based plasmid vectors of intermediate insert capacity, have now enabled the cloning of complete **herpesvirus** genomes. Infectious virus genomes can be shuttled between Escherichia coli and eukaryotic cells. **Herpesvirus BAC** DNA engineering in E. coli by homologous recombination requires neither restriction sites nor cloning steps and allows the introduction of a wide variety of DNA modifications. Such E. coli-based technology has provided a safe, fast and effective approach to the systematic mining of the information stored in **herpesvirus** genomes as a result of their intimate co-evolution with their specific hosts for millions of years. Use of this technique could lead to new developments in clinical virology and basic virology research, and increase the usage of viral genomes as investigative tools and vectors.

L27 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999224291 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10207884
TITLE: Rapid identification of essential and nonessential **herpesvirus** genes by direct transposon mutagenesis.
COMMENT: Comment in: Nat Biotechnol. 1999 Apr;17(4):332-3. PubMed ID: 10207876
AUTHOR: **Brune W**; Menard C; Hobom U; Odenbreit S; **Messerle M**; **Koszinowski U H**
CORPORATE SOURCE: Department of Virology, Max von Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, Germany.
SOURCE: Nature biotechnology, (1999 Apr) 17 (4) 360-4. Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990727
Last Updated on STN: 19990727
Entered Medline: 19990715

AB **Herpesviruses** are important pathogens in animals and humans. The large DNA genomes of several **herpesviruses** have been sequenced, but the function of the majority of putative genes is elusive. Determining which genes are essential for their replication is important for identifying potential chemotherapy targets, designing **herpesvirus** vectors, and generating attenuated vaccines. For this purpose, we recently reported that **herpesvirus** genomes can be maintained as infectious bacterial artificial chromosomes (**BAC**) in Escherichia coli. Here we describe a one-step procedure for random-insertion mutagenesis of a **herpesvirus BAC** using a Tn1721-based transposon system. Transposon insertion sites were determined by direct sequencing, and infectious virus was recovered by transfecting cultured cells with the mutant genomes. Lethal mutations were rescued by cotransfecting cells containing noninfectious genomes with the corresponding wild-type subgenomic fragments. We also constructed revertant genomes by allelic exchange in bacteria. These methods, which are generally applicable to any cloned **herpesvirus** genome, will facilitate analysis of gene function for this virus family.

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(FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005

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L2          537 S (MESSERLE, ?)/IN,AU
L3         5359 S (BRUNE, ?)/IN,AU
L4        43708 S (HAHN, ?)/IN,AU
L5            7 S L1 AND L2 AND L3 AND L4
L6            3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7        50178 S L1 OR L2 OR L3 OR L4
L8         5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9        16997 S BAC OR L8
L10      381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11         387 S L8 AND L10
L12          82 S L11 AND L7
L13       27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14         207 S L13 AND L8
L15          60 S L14 AND L7
L16          24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17          22 S L12 NOT L15
L18          12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19         305 S L11 NOT L12
L20           5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
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L21            2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)
L22        33498 S (MOSS, ?)/IN,AU OR  (DOMI, ?)/IN,AU
L23            0 S L19 AND L22
L24          557 S L9 AND L10
L25           93 S L24 AND L7
L26           11 S L25 NOT L12
L27            4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)

=> S L22 AND L24
L28            0 L22 AND L24

=> S L24 NOT L25
L29          464 L24 NOT L25

=> S (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU OR (OSTROVE,
?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L30         3618 (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU
                 OR (OSTROVE, ?)/IN,AU

=> S L30 AND L29
L31            7 L30 AND L29

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KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
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KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L31
L32            4 DUPLICATE REMOVE L31 (3 DUPLICATES REMOVED)

=> D IBIB AB L32 1-4

L32  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         1999:566208  CAPLUS
DOCUMENT NUMBER:          131:180806
TITLE:                    Artificial chromosome constructs containing nucleic
                          acid sequences capable of directing the formation of a
                          recombinant virus, and therapeutic uses thereof
INVENTOR(S):              Horsburgh, Brian; Qiang, Dong;
                          Tufaro, Francis; Ostrove, Jeffrey
PATENT ASSIGNEE(S):       Neurovir, Inc., Can.
SOURCE:                   PCT Int. Appl., 43 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 9943842            A1    19990902    WO 1999-IB285           19990129
         W:  AU, CA, JP
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     US 6277621            B1    20010821    US 1998-31006           19980226
     CA 2321964            AA    19990902    CA 1999-2321964         19990129
     AU 9922945            A1    19990915    AU 1999-22945           19990129
     AU 765521             B2    20030918
```

EP 1056878 A1 20001206 EP 1999-902747 19990129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002504382 T2 20020212 JP 2000-533581 19990129
US 6642207 B1 20031104 US 2001-922271 20010803
US 2004171569 A1 20040902 US 2003-701152 20031104
PRIORITY APPLN. INFO.: US 1998-31006 A 19980226
WO 1999-IB285 W 19990129
US 2001-922271 A1 20010803

AB The invention provides artificial chromosome constructs, DNA-based vectors that have been used extensively in the construction of DNA libraries, containing foreign nucleic acid sequences. The heterologous sequence is preferably viral in origin and encodes a therapeutic gene product, such as a growth factor, a hormone, an enzyme, a vaccine antigen, a cytotoxin, an immunomodulatory protein, an antisense RNA mol., or a ribozyme. In one embodiment of the invention, the artificial chromosome construct contains a nucleic acid sequence that directs formation of a recombinant lytic or non-lytic virus upon introduction into a cell. Depending upon the application, it may or may not be desirable that the recombinant virus produced upon introduction of an artificial chromosome construct into a cell kills said cell. The construct disclosed in the present invention (**HSV-BAC**-TK) comprises a bacterial artificial construct (**BAC**) with viral tk sequences flanking the signals necessary for chromosomal maintenance in bacteria and the chloramphenicol resistance gene, and **HSV**-1 infectious DNA. The invention also provides methods of using these artificial chromosome constructs for therapy and recombinant virus production

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 2000:398361 BIOSIS
DOCUMENT NUMBER: PREV200000398361
TITLE: Genetic manipulation of herpes simplex virus using bacterial artificial chromosomes.
AUTHOR(S): **Horsburgh, Brian C.** [Reprint author]; Hubinette, Maria M. [Reprint author]; **Tufaro, Frank** [Reprint author]
CORPORATE SOURCE: NeuroVir Inc., Vancouver, BC, V6T 1Z3, Canada
SOURCE: Glorioso, Joseph C.; Schmidt, Martin C. Methods Enzymol., (1999) pp. 337-352. Methods in Enzymology; Expression of recombinant genes in eukaryotic systems. print.
Publisher: Academic Press Inc., 525 B Street, Suite 1900, San Diego, CA, 92101-4495, USA; Academic Press Ltd., 24-28 Oval Road, London, NW1 7DX, UK. Series: Methods in Enzymology.
CODEN: MENZAU. ISSN: 0076-6879. ISBN: 0-12-182207-9 (cloth).
DOCUMENT TYPE: Book
Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Sep 2000
Last Updated on STN: 8 Jan 2002

L32 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 1999434743 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10505118
TITLE: Allele replacement: an application that permits rapid manipulation of herpes simplex virus type 1 genomes.
AUTHOR: **Horsburgh B C**; Hubinette M M; **Qiang D**; MacDonald M L; **Tufaro F**
CORPORATE SOURCE: NeuroVir Inc, Vancouver, BC, Canada.
SOURCE: Gene therapy, (1999 May) 6 (5) 922-30.
Journal code: 9421525. ISSN: 0969-7128.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991022

AB Herpes simplex virus (**HSV**) is a new platform for gene therapy. We cloned the human **herpesvirus HSV**-1 strain F genome into a **bacterial artificial chromosome** (**BAC**) and adapted chromosomal gene replacement technology to manipulate the viral genome. This technology exploits the power of bacterial genetics and permits generation of recombinant viruses in as few as 7 days. We utilized this technology to delete the viral packaging/cleavage (pac) sites from **HSV-BAC**. **HSV-BAC** DNA is stable in bacteria and the pac-deleted **HSV-BAC** (p45-25) is able to package amplicon plasmid DNA as efficiently as a comparable pac-deleted **HSV** cosmid set when transfected into mammalian cells. Moreover, the utility of bacterial gene replacement is not limited to **HSV**, since most **herpesviruses** can be cloned as BACs. Thus, this technology will greatly facilitate genetic manipulation of all **herpesviruses** for their use as research tools or as vectors in gene therapy.

L32 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:657733 CAPLUS
DOCUMENT NUMBER: 132:161777
TITLE: Genetic manipulation of herpes simplex virus using bacterial artificial chromosomes
AUTHOR(S): **Horsburgh, Brian C.**; Hubinette, Maria M.; **Tufaro, Frank**
CORPORATE SOURCE: NeuroVir Inc., Vancouver, BC, V6T 1Z3, Can.
SOURCE: Methods in Enzymology (1999), 306(Expression of Recombinant Genes in Eukaryotic Systems), 337-352
CODEN: MENZAU; ISSN: 0076-6879
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A seven-day procedure for making recombinant herpes simplex viruses using bacterial artificial chromosomes is presented. (c) 1999 Academic Press.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D HIS

(FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005

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L2          537 S (MESSERLE, ?)/IN,AU
L3         5359 S (BRUNE, ?)/IN,AU
L4        43708 S (HAHN, ?)/IN,AU
L5            7 S L1 AND L2 AND L3 AND L4
L6            3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7        50178 S L1 OR L2 OR L3 OR L4
L8         5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9        16997 S BAC OR L8
L10      381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11         387 S L8 AND L10
L12          82 S L11 AND L7
L13       27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14         207 S L13 AND L8
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L15          60 S L14 AND L7
L16          24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17          22 S L12 NOT L15
L18          12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19         305 S L11 NOT L12
L20           5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
L21           2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)
L22       33498 S (MOSS, ?)/IN,AU OR  (DOMI, ?)/IN,AU
L23           0 S L19 AND L22
L24         557 S L9 AND L10
L25          93 S L24 AND L7
L26          11 S L25 NOT L12
L27           4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)
L28           0 S L22 AND L24
L29         464 S L24 NOT L25
L30        3618 S (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU
L31           7 S L30 AND L29
L32           4 DUPLICATE REMOVE L31 (3 DUPLICATES REMOVED)

=> S L24 AND L30
L33           7 L24 AND L30

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?)/IN,AU OR (HAMMERSCHMIDT, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
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                U OR (ZEIDLER, ?)/IN,AU OR (HAMMERSCHMIDT, ?)/IN,AU

=> S L34 AND L24
L35           4 L34 AND L24

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DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L35
L36           1 DUPLICATE REMOVE L35 (3 DUPLICATES REMOVED)

=> D IBIB AB

L36  ANSWER 1 OF 1     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   1998070825     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9405686
TITLE:              Cloning and mutagenesis of a herpesvirus genome
                    as an infectious bacterial artificial
                    chromosome.
AUTHOR:             Messerle M; Crnkovic I; Hammerschmidt W; Ziegler
                    H; Koszinowski U H
CORPORATE SOURCE:   Max von Pettenkofer-Institut fur Hygiene und Mikrobiologie,
                    Ludwig-Maximilians-Universitat Munchen,
                    Feodor-Lynen-Strasse 25, D-81377 Munich, Germany..
                    Messerle@lmb.uni-muenchen.de
SOURCE:             Proceedings of the National Academy of Sciences of the
                    United States of America, (1997 Dec 23) 94 (26) 14759-63.
                    Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199802
ENTRY DATE:         Entered STN: 19980217
                    Last Updated on STN: 19980217
                    Entered Medline: 19980202
AB   A strategy for cloning and mutagenesis of an infectious
```

herpesvirus genome is described. The mouse **cytomegalovirus** genome was cloned and maintained as a 230 kb **bacterial artificial chromosome** (**BAC**) in E. coli. Transfection of the **BAC** plasmid into eukaryotic cells led to a productive virus infection. The feasibility to introduce targeted mutations into the **BAC** cloned virus genome was shown by mutation of the immediate-early 1 gene and generation of a mutant virus. Thus, the complete construction of a mutant **herpesvirus** genome can now be carried out in a controlled manner prior to the reconstitution of infectious progeny. The described approach should be generally applicable to the mutagenesis of genomes of other large DNA viruses.

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=> D HIS

     (FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
L1           802 S (KOSZINOWSKI, ?)/IN,AU
L2           537 S (MESSERLE, ?)/IN,AU
L3          5359 S (BRUNE, ?)/IN,AU
L4         43708 S (HAHN, ?)/IN,AU
L5             7 S L1 AND L2 AND L3 AND L4
L6             3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7         50178 S L1 OR L2 OR L3 OR L4
L8          5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9         16997 S BAC OR L8
L10       381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11          387 S L8 AND L10
L12           82 S L11 AND L7
L13        27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14          207 S L13 AND L8
L15           60 S L14 AND L7
L16           24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17           22 S L12 NOT L15
L18           12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19          305 S L11 NOT L12
L20            5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
L21            2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)
L22        33498 S (MOSS, ?)/IN,AU OR  (DOMI, ?)/IN,AU
L23            0 S L19 AND L22
L24          557 S L9 AND L10
L25           93 S L24 AND L7
L26           11 S L25 NOT L12
L27            4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)
L28            0 S L22 AND L24
L29          464 S L24 NOT L25
L30         3618 S (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU
L31            7 S L30 AND L29
L32            4 DUPLICATE REMOVE L31 (3 DUPLICATES REMOVED)
L33            7 S L24 AND L30
L34         6767 S (DELECLUSE, ?)/IN,AU OR (HILSENDEGEN, ?)/IN,AU OR (PICH, ?)/I
L35            4 S L34 AND L24
L36            1 DUPLICATE REMOVE L35 (3 DUPLICATES REMOVED)

=> S  (HAMMERSCHMIDT, ?)/IN,AU AND ((BRIELMEIER, ?)/IN,AU OR (KILGER, ?)/IN,AU OR
(KEMPKES, ?)/IN,AU)
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L37           55 (HAMMERSCHMIDT, ?)/IN,AU AND ((BRIELMEIER, ?)/IN,AU OR (KILGER,
                 ?)/IN,AU OR (KEMPKES, ?)/IN,AU)

=> S L37 AND L10
L38           34 L37 AND L10
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=> S L38 AND PY<1999
   1 FILES SEARCHED...
   3 FILES SEARCHED...
L39          24 L38 AND PY<1999

=> DUPLICATE REMOVE L39
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L39
L40          14 DUPLICATE REMOVE L39 (10 DUPLICATES REMOVED)

=> D IBIB AB L40 1-14

L40  ANSWER 1 OF 14     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   1998169386     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9501091
TITLE:              Epstein-Barr virus-mediated B-cell proliferation is
                    dependent upon latent membrane protein 1, which simulates
                    an activated CD40 receptor.
AUTHOR:             Kilger E; Kieser A; Baumann M; Hammerschmidt
                    W
CORPORATE SOURCE:   GSF-National Research Center for Environment and Health,
                    Institut f r Klinische Molekularbiologie und Tumorgenetik,
                    Marchioninistr. 25, D-81377 Munich, Germany.
CONTRACT NUMBER:    AI-29988 (NIAID)
SOURCE:             EMBO journal, (1998 Mar 16) 17 (6) 1700-9.
                    Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY:       ENGLAND: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199804
ENTRY DATE:         Entered STN: 19980507
                    Last Updated on STN: 19980507
                    Entered Medline: 19980424
AB   The Epstein-Barr virus (EBV) latent membrane protein 1 (LMP1) is essential
     for the immortalization of human B cells and is linked etiologically to
     several human tumors. LMP1 is an integral membrane protein which acts
     like a constitutively active receptor. It binds tumor necrosis factor
     (TNF)-receptor-associated factors (TRAFs), activates NF-kappaB and
     triggers the transcription factor AP-1 via the c-Jun N-terminal kinase
     (JNK) cascade, but its specific contribution to B-cell immortalization has
     not been elucidated fully. To address the function of LMP1, we
     established B cell lines with a novel mini-EBV plasmid in which the LMP1
     gene can be regulated at will without affecting the expression of other
     latent EBV genes. We demonstrate here that continuous expression of LMP1
     is essential for the proliferation of EBV-immortalized B cells in vitro.
     Re-induction of LMP1 expression or activation of the cellular CD40
     receptor both induce the JNK signaling cascade, activate the transcription
     factor NF-kappaB and stimulate proliferation of these B cells. Our
     findings strongly suggest that LMP1 mimics B-cell activation processes
     which are physiologically triggered by CD40-CD40 ligand signals. Since
     LMP1 acts in a ligand-independent manner, it replaces the T cell-derived
     activation signal to sustain indefinite B-cell proliferation.

L40  ANSWER 2 OF 14     MEDLINE on STN                    DUPLICATE 2
ACCESSION NUMBER:   1998062995     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9351829
TITLE:              Epstein-Barr virus latent membrane protein-1 triggers AP-1
                    activity via the c-Jun N-terminal kinase cascade.
AUTHOR:             Kieser A; Kilger E; Gires O; Ueffing M; Kolch W;
                    Hammerschmidt W
CORPORATE SOURCE:   GSF-National Research Center for Environment and Health,
```

Institute for Clinical Molecular Biology and Tumor Genetics, Munchen, Germany.
SOURCE: EMBO journal, **(1997 Nov 3)** 16 (21) 6478-85.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980122
Last Updated on STN: 20000303
Entered Medline: 19980108

AB The Epstein-Barr virus latent membrane protein-1 (LMP-1) is an integral membrane protein which transforms fibroblasts and is essential for EBV-mediated B-cell immortalization. LMP-1 has been shown to trigger cellular NF-kappa B activity which, however, cannot fully explain the oncogenic potential of LMP-1. Here we show that LMP-1 induces the activity of the AP-1 transcription factor, a dimer of Jun/Jun or Jun/Fos proteins. LMP-1 effects on AP-1 are mediated through activation of the c-Jun N-terminal kinase (JNK) cascade, but not the extracellular signal-regulated kinase (Erk) pathway. Consequently, LMP-1 triggers the activity of the c-Jun N-terminal transactivation domain which is known to be activated upon JNK-mediated phosphorylation. Deletion analysis indicates that the 55 C-terminal amino acids of the LMP-1 molecule, but not its TRAF interaction domain, are essential for AP-1 activation. JNK-mediated transcriptional activation of AP-1 is the direct output of LMP-1-triggered signaling, as shown by an inducible LMP-1 mutant. Using a tetracycline-regulated LMP-1 allele, we demonstrate that JNK is also an effector of non-cytotoxic LMP-1 signaling in B cells, the physiological target cells of EBV. In summary, our data reveal a novel effector of LMP-1, the SEK/JNK/c-Jun/AP-1 pathway, which contributes to our understanding of the immortalizing and transforming potential of LMP-1.

L40 ANSWER 3 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1997:379140 BIOSIS
DOCUMENT NUMBER: PREV199799678343
TITLE: EBV, c-myc, and Burkitt's lymphoma.
AUTHOR(S): Polack, A. [Reprint author]; **Kempkes, B.**; Strobl, L.; Zimber-Strobl, U.; Ueffing, M.; Hoertnagel, K.; Geltinger, C. [Reprint author]; **Hammerschmidt, W.** [Reprint author]; Bornkamm, G. W.
CORPORATE SOURCE: Inst. Klinische Molekularobiolgie Tumorgenetik, GSF-Forschungszentrum Umwelt Gesundheit, Marchioninistr. 25, 81377 Muenchen, Germany
SOURCE: Journal of Molecular Medicine (Berlin), (1997) Vol. 75, No. 7, pp. B165.
Meeting Info.: XIX Symposium of the International Association for Comparative Research on Leukemia and Related Diseases. Heidelberg, Germany. July 13-18, 1997.
ISSN: 0946-2716.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 1997
Last Updated on STN: 4 Sep 1997

L40 ANSWER 4 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN DUPLICATE 3
ACCESSION NUMBER: 1997:74316 BIOSIS
DOCUMENT NUMBER: PREV199799381019
TITLE: Epstein-Barr virus latent membrane protein (LMP1) is not sufficient to maintain proliferation of B cells but both it and activated CD40 can prolong their survival.

AUTHOR(S): Zimber-Strobl, Ursula; **Kempkes, Bettina**; Marschall, Gabriele; Zeidler, Reinhard; Van Kooten, Cees; Banchereau, Jacques; Bornkamm, Georg W.; **Hammerschmidt, Wolfgang** [Reprint author]
CORPORATE SOURCE: GSF-Natl. Res. Cent. Environ. Health, Institut fuer Klinische Molekularbiologie und Tumorgenetik, Haematologikum, Marchioninistrasse 25, D-81377 Muenchen, Germany
SOURCE: EMBO (European Molecular Biology Organization) Journal, (1996) Vol. 15, No. 24, pp. 7070-7078.
CODEN: EMJODG. ISSN: 0261-4189.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Feb 1997
Last Updated on STN: 26 Feb 1997

AB Epstein-Barr virus (EBV) infects human primary B lymphocytes and induces and maintains proliferation of these cells efficiently in vitro. Mutants of Epstein-Barr virus which express EBV nuclear antigen 2 (EBNA2) in a conditional fashion allow dissection of individual contributions of viral genes to B cell immortalization. EBNA2 is a transcriptional activator of cellular and viral genes, including the viral latent membrane protein 1 (LMP1), which is essential for B cell immortalization and has oncogenic effects in nonlymphoid cells. To analyze the role of this gene in B cell immortalization, LMP1 was constitutively expressed in B cells infected with EBV carrying a conditional EBNA2 allele. In the absence of functional EBNA2, LMP1 was incapable of sustaining B cell proliferation in two independent assays but induced a phenotype consistent with prolonged cell viability. Activation of CD40 displayed a comparable phenotype. These data indicate that both CD40 activation and LMP1 expression may use a common pathway for B cell activation. Proliferation of human B cells, however, requires one or more additional signals triggered by EBNA2.

L40 ANSWER 5 OF 14 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 97081193 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8922475
TITLE: The latent membrane protein 2 gene of Epstein-Barr virus is important for efficient B cell immortalization.
AUTHOR: **Brielmeier M**; Mautner J; Laux G; **Hammerschmidt W**
CORPORATE SOURCE: Institut fur Klinische Molekularbiologie und Tumorgenetik, GSF-Forschungszentrum fur Umwelt und Gesundheit GmbH, Munchen, Germany.
CONTRACT NUMBER: AI-29988 (NIAID)
SOURCE: Journal of general virology, **(1996 Nov)** 77 (Pt 11) 2807-18.
Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961219

AB The viral latent membrane proteins 2 (LMP2) of Epstein-Barr virus (EBV) were analysed genetically to evaluate their role in B cell immortalization. LMP2 is transcribed as two differently spliced mRNAs which code for the LMP2A and -B proteins, also called terminal protein-1 and -2. LMP2A and -B are found in latently infected, growth-transformed B lymphocytes in vitro, in different human tumours, and in latently infected B cells in vivo. Two different approaches were used to generate EBV mutants in which the second, third and part of the fourth exon of the LMP2 gene were deleted by insertion of a marker gene. Initially, conventional homologous recombination in a Burkitt's lymphoma cell line (P3HR1) between

the endogenous EBV genome and an introduced plasmid was used to generate EBV mutants. This experiment identified LMP2 as dispensable for B cell immortalization as has been reported. In a second approach, the same LMP2 mutant gene was analysed in the context of a mini-EBV plasmid. These are E. coli constructs that are sufficient when packaged into an EBV coat both to initiate and to maintain proliferation of infected B cells. In comparison with a fully competent mini-EBV, LMP2- mini-EBVs were found to be greatly reduced in their capacity to yield immortalized B cell clones. This finding confirmed the initially observed bias against LMP2- B cell clones, most of which were found to be coinfected with complementing P3HR1 virus. These results indicate that LMP2 contributes to the efficiency of B cell immortalization and that the LMP2s phenotype is auxiliary in nature.

L40 ANSWER 6 OF 14 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 96226361 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8649832
TITLE: c-myc expression is activated by the immunoglobulin kappa-enhancers from a distance of at least 30 kb but not by elements located within 50 kb of the unaltered c-myc locus in vivo.
AUTHOR: Mautner J; Behrends U; Hortnagel K; **Brielmeier M**; **Hammerschmidt W**; Strobl L; Bornkamm G W; Polack A
CORPORATE SOURCE: Institut fur Klinische Molekularbiologie und Tumorgenetik, GSF-Forschungszentrum fur Umwelt und Gesundheit GmbH, Munchen, Germany.
SOURCE: Oncogene, **(1996 Mar 21)** 12 (6) 1299-307.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960805
Last Updated on STN: 19980206
Entered Medline: 19960725

AB 50 kb of contiguous DNA sequences covering the human c-myc coding region and approximately 20 kb of flanking upstream and downstream sequences were cloned onto a prokaryotic F-factor derived plasmid, which also contains a selectable marker and the plasmid origin of DNA replication oriP of Epstein Barr virus (EBV). Since these plasmids replicate extrachromosomally after stable transfection into EBV-positive B-cell lines, the gene regulation of c-myc can be analysed independent from chromosomal integration positions. Despite the presence of all known c-myc regulatory elements on these constructs, expression from the stably transfected c-myc gene was barely detectable in either cell line. Hypermethylation of these plasmids could be excluded as a mechanism for the lack of gene expression. Insertion of the immunoglobulin kappa-intron and 3' enhancers, however, activated c-myc transcription, when placed adjacent to or separated from the c-myc promoters by as far as 30 kb. These results indicate that transcription of c-myc in vivo requires additional and still unidentified control elements located outside this 50 kb fragment, and experimentally demonstrate long range enhancer function in vivo.

L40 ANSWER 7 OF 14 BIOSIS on STN
ACCESSION NUMBER: 1996:393095 BIOSIS
DOCUMENT NUMBER: PREV199699115451
TITLE: Studies on the role of the latent membrane proteins 2 of Epstein Barr virus in B cell immortalization.
AUTHOR(S): **Brielmeier, Markus** [Reprint author]; Mautner, Josef [Reprint author]; Laux, Gerhard [Reprint author]; **Hammerschmidt, Wolfgang**

CORPORATE SOURCE: GSF-Forschungszentrum Umwelt und Gesundheit GmbH, D-81377 Muenchen, Germany
SOURCE: British Journal of Haematology, (1996) Vol. 93, No. SUPPL. 2, pp. 280.
Meeting Info.: Second Meeting of the European Haematology Association. Paris, France. May 29-June 1, 1996.
CODEN: BJHEAL. ISSN: 0007-1048.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Sep 1996
Last Updated on STN: 3 Sep 1996

L40 ANSWER 8 OF 14 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 96226013 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8627226
TITLE: Epstein-Barr virus nuclear antigen 2 (EBNA2)-oestrogen receptor fusion proteins complement the EBNA2-deficient Epstein-Barr virus strain P3HR1 in transformation of primary B cells but suppress growth of human B cell lymphoma lines.
AUTHOR: **Kempkes B**; Zimber-Strobl U; Eissner G; Pawlita M; Falk M; **Hammerschmidt W**; Bornkamm G W
CORPORATE SOURCE: GSF-Forschungszentrum fur Umwelt und Gesundheit, Institut fur Molekularbiologie und Tumorgenetik, Munchen, Germany.
SOURCE: Journal of general virology, **(1996 Feb)** 77 (Pt 2) 227-37.
Journal code: 0077340. ISSN: 0022-1317.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960708
Last Updated on STN: 19960708
Entered Medline: 19960627

AB To develop a transformation system with a conditional Epstein-Barr virus nuclear antigen 2 (EBNA2) gene, we fused the hormone binding domain of the oestrogen receptor to the N or C terminus of EBNA2. In promoter transactivation as well as primary B cell transformation assays these chimeric EBNA2 proteins are able to substitute for wild-type EBNA2 in the presence of oestrogen. Here we provide evidence that this transformation is the result of double infection of a cell with two virions, the P3HR1 virus genome and a mini-EBV plasmid carrying the chimeric EBNA2 gene. Unexpectedly, expression of the same EBNA2-oestrogen receptor fusion protein in established human B cell lymphoma lines resulted in growth retardation or growth arrest upon the addition of oestrogen. By titrating the oestrogen concentration in these stably transfected cells, the growth retarding and the transactivating function of the chimeric proteins could not be dissociated. We propose that growth inhibition of established B cell lymphoma lines is a novel function of EBNA2 which has not been detected in the absence of an inducible system. It remains open whether the growth retarding property of the EBNA2-oestrogen receptor fusion protein in B cell lymphoma lines is due to unphysiologically high expression of the chimeric protein or to interference with a cellular programme driving proliferation in these cell lines.

L40 ANSWER 9 OF 14 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 95320178 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7597045
TITLE: Immortalization of human primary B lymphocytes in vitro with DNA.
AUTHOR: **Kempkes B**; Pich D; Zeidler R; **Hammerschmidt**

W
CORPORATE SOURCE: Institut fur Klinische Molekularbiologie und Tumorgenetik, GSF-Forschungszentrum fur Umwelt und Gesundheit GmbH, Munich, Germany.
CONTRACT NUMBER: AI-29988 (NIAID)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, **(1995 Jun 20)** 92 (13) 5875-9.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950817
Last Updated on STN: 19950817
Entered Medline: 19950803

AB Epstein-Barr virus (EBV) is a human DNA tumor virus that efficiently immortalizes human primary B lymphocytes in vitro. Although viral genes that are expressed in latently infected B lymphocytes have been shown to function in cellular growth control, their detailed genetic analysis has been cumbersome for two reasons. The viral genome is too large to permit genetic engineering and human primary B lymphocytes, the only targets for infection by EBV in vitro, are both intractable in culture and recalcitrant to DNA transfection. To overcome these obstacles, we have assembled all the essential genes of EBV on a single recombinant vector molecule in Escherichia coli. We show here that this mini-EBV plasmid can yield immortalized B cells upon transfer of its naked DNA into human primary B lymphocytes. Established cell lines carry recombinant vector DNA and cannot support virus production. Because this DNA can be easily manipulated in E. coli, mutant mini-EBVs as well as foreign genes can now be introduced and studied successfully in recipient B lymphocytes from any human donors. These mini-EBVs therefore are potentially useful for human gene therapy.

L40 ANSWER 10 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
ACCESSION NUMBER: 1995:279640 BIOSIS
DOCUMENT NUMBER: PREV199598293940
TITLE: Epstein-Barr virus-derived plasmids as shuttle-vectors for gene therapy.
AUTHOR(S): Zeidler, Reinhard; **Kempkes, Bettina**; Pich, Dagmar; **Hammerschmidt, Wolfgang**
CORPORATE SOURCE: Inst. Klinische Molekularbiol. Tumorgenetik, GSF-Forschungszentrum Umwelt Gesundheit GmbH, Marchioninistrasse 25, 81377 Muenchen, Germany
SOURCE: Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 21A, pp. 416.
Meeting Info.: Keystone Symposium on Gene Therapy and Molecular Medicine. Steamboat Springs, Colorado, USA. March 26-April 1, 1995.
ISSN: 0733-1959.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jul 1995
Last Updated on STN: 5 Jul 1995

L40 ANSWER 11 OF 14 MEDLINE on STN
ACCESSION NUMBER: 95074870 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7983714
TITLE: Immortalization of human B lymphocytes by a plasmid containing 71 kilobase pairs of Epstein-Barr virus DNA.

AUTHOR: **Kempkes B**; Pich D; Zeidler R; Sugden B; **Hammerschmidt W**
CORPORATE SOURCE: Institut fur Klinische Molekularbiologie und Tumorgenetik, GSF-Forschungszentrum fur Umwelt und Gesundheit GmbH, Munich, Germany.
CONTRACT NUMBER: AI-29988 (NIAID)
CA-07175 (NCI)
CA-22443 (NCI)
SOURCE: Journal of virology, **(1995 Jan)** 69 (1) 231-8.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950116
Last Updated on STN: 19950116
Entered Medline: 19950105

AB We have assembled derivatives of Epstein-Barr Virus (EBV) that include 71 kbp of noncontiguous DNA sequences cloned into a prokaryotic F-factor plasmid. These mini-EBVs, when introduced into an EBV-containing lymphoblastoid cell, can be packaged by the endogenous helper virus. One such mini-EBV was found to have a single C residue deleted from its EBNA3a open reading frame. When packaged, this mini-EBV initiates proliferation of infected primary human B lymphocytes only in conjunction with a complementing helper virus. Proliferation of the infected cells, however, was maintained either alone by the mini-EBV containing the mutated EBNA3a open reading frame or alone by its derivative in which the EBNA3a open reading frame had been healed of its lesion by recombination with the helper virus. The mini-EBV with a wild-type EBNA3a open reading frame when packaged alone can both initiate and maintain proliferation upon infection of primary human B lymphocytes. These findings identify 41% of EBV DNA which is sufficient to immortalize primary human B lymphocytes and provide an assay to distinguish virus contributions to initiation or maintenance of cell proliferation or both. They also identify EBNA3a as a transforming gene, which contributes primarily to the initiation of cell proliferation.

L40 ANSWER 12 OF 14 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 95129555 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7828599
TITLE: B-cell proliferation and induction of early G1-regulating proteins by Epstein-Barr virus mutants conditional for EBNA2.
AUTHOR: **Kempkes B**; Spitkovsky D; Jansen-Durr P; Ellwart J W; Kremmer E; Delecluse H J; Rottenberger C; Bornkamm G W; **Hammerschmidt W**
CORPORATE SOURCE: Institut fur Klinische Molekularbiologie und Tumorgenetik, Munchen, Germany.
SOURCE: EMBO journal, **(1995 Jan 3)** 14 (1) 88-96.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950307
Last Updated on STN: 19950307
Entered Medline: 19950217

AB Infection of primary B-lymphocytes by Epstein-Barr virus (EBV) leads to growth transformation of these B-cells in vitro. EBV nuclear antigen 2 (EBNA2), one of the first genes expressed after EBV infection of B-cells, is a transcriptional activator of viral and cellular genes and is essential for the transforming potential of the virus. We generated

conditional EBV mutants by expressing EBNA2 as chimeric fusion protein with the hormone binding domain of the estrogen receptor on the genetic background of the virus. Growth transformation of primary normal B-cells by mutant virus resulted in estrogen-dependent lymphoblastoid cell lines expressing the chimeric EBNA2 protein. In the absence of estrogen about half of the cells enter a quiescent non-proliferative state whereas the others die by apoptosis. EBNA2 is thus required not only for initiation but also for maintenance of transformation. Growth arrest occurred at G1 and G2 stages of the cell cycle, indicating that functional EBNA2 is required at different restriction points of the cell cycle. Growth arrest is reversible for G1/G0 cells as indicated by the sequential accumulation and modification of cell cycle regulating proteins. EBV induces the same cell cycle regulating proteins as polyclonal stimuli in primary B-cells. These data suggest that EBV is using a common pathway for B-cell activation bypassing the requirement for antigen, T-cell signals and growth factors.

L40 ANSWER 13 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 1995:65665 BIOSIS
DOCUMENT NUMBER: PREV199598079965
TITLE: Immortalization of human B lymphocytes by a plasmid containing 71 kilobase pairs of Epstein-Barr virus DNA.
AUTHOR(S): **Kempkes, Bettina**; Pich, Dagmar; Zeidler, Reinhard; Sugden, Bill; **Hammerschmidt, Wolfgang** [Reprint author]
CORPORATE SOURCE: Inst. Klinische Molekularbiologie Tumorgenetik, GSF-Forschungszentrum Umwelt und Gesundheit GmbH, D-81377 Muenchen, Germany
SOURCE: Journal of Virology, (1994) Vol. 69, No. 1, pp. 231-238. CODEN: JOVIAM. ISSN: 0022-538X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Feb 1995
Last Updated on STN: 8 Feb 1995

AB We have assembled derivatives of Epstein-Barr Virus (EBV) that include 71 kbp of noncontiguous DNA sequences cloned into a prokaryotic F-factor plasmid. These mini-EBVs, when introduced into an EBV-containing lymphoblastoid cell, can be packaged by the endogenous helper virus. One such mini-EBV was found to have a single C residue deleted from its EBNA3a open reading frame. When packaged, this mini-EBV initiates proliferation of infected primary human B lymphocytes only in conjunction with a complementing helper virus. Proliferation of the infected cells, however, was maintained either alone by the mini-EBV containing the mutated EBNA3a open reading frame or alone by its derivative in which the EBNA3a open reading frame had been healed of its lesion by recombination with the helper virus. The mini-EBV with a wild-type EBNA3a open reading frame when packaged alone can both initiate and maintain proliferation upon infection of primary human B lymphocytes. These findings identify 41% of EBV DNA which is sufficient to immortalize primary human B lymphocytes and provide an assay to distinguish virus contributions to initiation or maintenance of cell proliferation or both. They also identify EBNA3a as a transforming gene, which contributes primarily to the initiation of cell proliferation.

L40 ANSWER 14 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 1994:204062 BIOSIS
DOCUMENT NUMBER: PREV199497217062
TITLE: Epstein-Barr virus nuclear antigen 2 function is required for maintenance of Epstein-Barr virus induced B-cell transformation.
AUTHOR(S): **Kempkes, Bettina** [Reprint author]; Delecluse, Henri-Jacques [Reprint author]; Rottenberger, Christine

[Reprint author]; Kremmer, Elisabeth; Bornkamm, Georg W.
[Reprint author]; **Hammerschmidt, Wolfgang**
[Reprint author]

CORPORATE SOURCE: GSF - Forschungszentrum Umwelt Gesundheit, Muenchen, Germany

SOURCE: Journal of Cellular Biochemistry Supplement, (1994) Vol. 0, No. 18C, pp. 231.
Meeting Info.: Keystone Symposium on Human Tumor Viruses. Taos, New Mexico, USA. February 13-20, 1994.
ISSN: 0733-1959.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 May 1994
Last Updated on STN: 2 May 1994

=> D HIS

(FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005

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L1          802 S (KOSZINOWSKI, ?)/IN,AU
L2          537 S (MESSERLE, ?)/IN,AU
L3         5359 S (BRUNE, ?)/IN,AU
L4        43708 S (HAHN, ?)/IN,AU
L5            7 S L1 AND L2 AND L3 AND L4
L6            3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7        50178 S L1 OR L2 OR L3 OR L4
L8         5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9        16997 S BAC OR L8
L10      381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11         387 S L8 AND L10
L12          82 S L11 AND L7
L13       27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14         207 S L13 AND L8
L15          60 S L14 AND L7
L16          24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17          22 S L12 NOT L15
L18          12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19         305 S L11 NOT L12
L20           5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
L21           2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)
L22       33498 S (MOSS, ?)/IN,AU OR  (DOMI, ?)/IN,AU
L23           0 S L19 AND L22
L24         557 S L9 AND L10
L25          93 S L24 AND L7
L26          11 S L25 NOT L12
L27           4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)
L28           0 S L22 AND L24
L29         464 S L24 NOT L25
L30        3618 S (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU
L31           7 S L30 AND L29
L32           4 DUPLICATE REMOVE L31 (3 DUPLICATES REMOVED)
L33           7 S L24 AND L30
L34        6767 S (DELECLUSE, ?)/IN,AU OR (HILSENDEGEN, ?)/IN,AU OR (PICH, ?)/I
L35           4 S L34 AND L24
L36           1 DUPLICATE REMOVE L35 (3 DUPLICATES REMOVED)
L37          55 S  (HAMMERSCHMIDT, ?)/IN,AU AND ((BRIELMEIER, ?)/IN,AU OR (KILG
L38          34 S L37 AND L10
L39          24 S L38 AND PY<1999
L40          14 DUPLICATE REMOVE L39 (10 DUPLICATES REMOVED)
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=> S (STAVROPOULOS, ?)/IN,AU OR (STRATHDEE, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L41       2043 (STAVROPOULOS, ?)/IN,AU OR (STRATHDEE, ?)/IN,AU

=> S (STAVROPOULOS, ?)/IN,AU AND (STRATHDEE, ?)/IN,AU
'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L42         14 (STAVROPOULOS, ?)/IN,AU AND (STRATHDEE, ?)/IN,AU

=> S L41 AND L24
L43          4 L41 AND L24

=> DUPLICATE REMOVE L43
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L43
L44           1 DUPLICATE REMOVE L43 (3 DUPLICATES REMOVED)

=> D IBIB AB L44

L44  ANSWER 1 OF 1     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   1998362116     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 9696807
TITLE:              An enhanced packaging system for helper-dependent herpes
                    simplex virus vectors.
AUTHOR:             Stavropoulos T A; Strathdee C A
CORPORATE SOURCE:   Gene Therapy and Molecular Virology Group, The John P.
                    Robarts Research Institute, London, Ontario, Canada N6A
                    5K8.
SOURCE:             Journal of virology, (1998 Sep) 72 (9) 7137-43.
                    Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199809
ENTRY DATE:         Entered STN: 19980925
                    Last Updated on STN: 19980925
                    Entered Medline: 19980916
AB   Helper-dependent herpes simplex virus (HSV) vectors (amplicons)
     show considerable promise to provide for long-term transduced-gene
     expression in most cell types.  The current packaging system of choice for
     these vectors involves cotransfection with a set of five overlapping
     cosmids that encode the full HSV type 1 (HSV-1) helper
     virus genome from which the packaging (pac) elements have been deleted.
     Although both the helper virus and the HSV amplicon can
     replicate, only the latter is packaged into infectious viral particles.
     Since the titers obtained are too low for practical application, an
     enhanced second-generation packaging system was developed by modifying
     both the helper virus and the HSV amplicon vector.  The helper
     virus was reverse engineered by using the original five cosmids to
     generate a single HSV-bacterial artificial
     chromosome (BAC) clone in Escherichia coli from which
     the pac elements were deleted to generate a replication-proficient but
     packaging-defective HSV-1 genome.  The HSV amplicon
     was modified to contain the simian virus 40 origin of replication, which
     acts as an HSV-independent replicon to provide for the
     replicative expansion of the vector.  The HSV amplicon is
     packaged into infectious particles by cotransfection with the HSV
     -BAC helper virus into the 293T cell line, and the resulting
     cell lysate is free of detectable helper virus contamination.  The
     combination of both modifications to the original packaging system affords
     an eightfold increase in the packaged-vector yield.
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     (FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
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L2           537 S (MESSERLE, ?)/IN,AU
L3          5359 S (BRUNE, ?)/IN,AU
L4         43708 S (HAHN, ?)/IN,AU
L5             7 S L1 AND L2 AND L3 AND L4
L6             3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7         50178 S L1 OR L2 OR L3 OR L4
L8          5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9         16997 S BAC OR L8
L10       381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11          387 S L8 AND L10
L12           82 S L11 AND L7
L13        27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14          207 S L13 AND L8
L15           60 S L14 AND L7
L16           24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17           22 S L12 NOT L15
L18           12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19          305 S L11 NOT L12
L20            5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
L21            2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)
L22        33498 S (MOSS, ?)/IN,AU OR  (DOMI, ?)/IN,AU
L23            0 S L19 AND L22
L24          557 S L9 AND L10
L25           93 S L24 AND L7
L26           11 S L25 NOT L12
L27            4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)
L28            0 S L22 AND L24
L29          464 S L24 NOT L25
L30         3618 S (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU
L31            7 S L30 AND L29
L32            4 DUPLICATE REMOVE L31 (3 DUPLICATES REMOVED)
L33            7 S L24 AND L30
L34         6767 S (DELECLUSE, ?)/IN,AU OR (HILSENDEGEN, ?)/IN,AU OR (PICH, ?)/I
L35            4 S L34 AND L24
L36            1 DUPLICATE REMOVE L35 (3 DUPLICATES REMOVED)
L37           55 S  (HAMMERSCHMIDT, ?)/IN,AU AND ((BRIELMEIER, ?)/IN,AU OR (KILG
L38           34 S L37 AND L10
L39           24 S L38 AND PY<1999
L40           14 DUPLICATE REMOVE L39 (10 DUPLICATES REMOVED)
L41         2043 S (STAVROPOULOS, ?)/IN,AU OR (STRATHDEE, ?)/IN,AU
L42           14 S (STAVROPOULOS, ?)/IN,AU AND (STRATHDEE, ?)/IN,AU
L43            4 S L41 AND L24
L44            1 DUPLICATE REMOVE L43 (3 DUPLICATES REMOVED)

=> S L41 AND L10
L45           39 L41 AND L10

=> S L45 NOT L43
L46           35 L45 NOT L43

=> DUPLICATE REMOVE L46
DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):N
PROCESSING COMPLETED FOR L46
L47           18 DUPLICATE REMOVE L46 (17 DUPLICATES REMOVED)
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=> D TI L47 1-18

L47 ANSWER 1 OF 18 MEDLINE on STN DUPLICATE 1
TI A conditionally replicating **adenovirus** for nasopharyngeal carcinoma gene therapy.

L47 ANSWER 2 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI A novel conditionally oncolytic **adenovirus** for the treatment of nasopharyngeal carcinoma (NPC).

L47 ANSWER 3 OF 18 MEDLINE on STN DUPLICATE 2
TI Tumor-targeted gene therapy for nasopharyngeal carcinoma.

L47 ANSWER 4 OF 18 MEDLINE on STN DUPLICATE 3
TI Biolistic-mediated interleukin 4 gene transfer prevents the onset of type 1 diabetes.

L47 ANSWER 5 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI Immunotherapy of spontaneous type 1 diabetes in NOD mice by systemic interleukin-4 treatment employing biolistic plasmid DNA and **adenovirus** vector-mediated gene transfer.

L47 ANSWER 6 OF 18 MEDLINE on STN DUPLICATE 4
TI A modular set of helper-dependent herpes simplex virus expression vectors.

L47 ANSWER 7 OF 18 MEDLINE on STN DUPLICATE 5
TI Herpes simplex viral and amplicon vector-mediated gene transfer into glia and neurons in organotypic spinal cord and dorsal root ganglion cultures.

L47 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
TI Stable gene transfer using hybrid herpes simplex-epstein-barr virus amplicon vectors

L47 ANSWER 9 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI The development of a novel Epstein Barr-Virus targeted **adenoviral** vector for cancer gene therapy.

L47 ANSWER 10 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI The development of a novel Epstein Barr virus-targeted **adenoviral** vector for cancer gene therapy.

L47 ANSWER 11 OF 18 MEDLINE on STN
TI Transposing BACs to the future.

L47 ANSWER 12 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI UV-enhanced reactivation of a UV-damaged reporter gene is promoter specific in human cells.

L47 ANSWER 13 OF 18 MEDLINE on STN DUPLICATE 6
TI Efficient control of tetracycline-responsive gene expression from an autoregulated bi-directional expression vector.

L47 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
TI Hybrid herpes simplex virus/Epstein-Barr virus vectors for heterologous gene delivery and expression

L47 ANSWER 15 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation. on STN
TI **HSV** amplicon vectors infect neurons of spinal cord organotypic

slice cultures and dorsal root ganglia in vivo.

L47 ANSWER 16 OF 18 MEDLINE on STN DUPLICATE 7
TI A decade of research on the natural history of HIV infection: Part 2. Cofactors.

L47 ANSWER 17 OF 18 MEDLINE on STN
TI The epidemiology of HIV-associated Kaposi's sarcoma: the unraveling mystery.

L47 ANSWER 18 OF 18 MEDLINE on STN DUPLICATE 8
TI The changing spectrum of AIDS index diseases in Canada.

=> D HIS

(FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
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L7 50178 S L1 OR L2 OR L3 OR L4
L8 5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
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L13 27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14 207 S L13 AND L8
L15 60 S L14 AND L7
L16 24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17 22 S L12 NOT L15
L18 12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19 305 S L11 NOT L12
L20 5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
L21 2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)
L22 33498 S (MOSS, ?)/IN,AU OR (DOMI, ?)/IN,AU
L23 0 S L19 AND L22
L24 557 S L9 AND L10
L25 93 S L24 AND L7
L26 11 S L25 NOT L12
L27 4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)
L28 0 S L22 AND L24
L29 464 S L24 NOT L25
L30 3618 S (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU
L31 7 S L30 AND L29
L32 4 DUPLICATE REMOVE L31 (3 DUPLICATES REMOVED)
L33 7 S L24 AND L30
L34 6767 S (DELECLUSE, ?)/IN,AU OR (HILSENDEGEN, ?)/IN,AU OR (PICH, ?)/I
L35 4 S L34 AND L24
L36 1 DUPLICATE REMOVE L35 (3 DUPLICATES REMOVED)
L37 55 S (HAMMERSCHMIDT, ?)/IN,AU AND ((BRIELMEIER, ?)/IN,AU OR (KILG
L38 34 S L37 AND L10
L39 24 S L38 AND PY<1999
L40 14 DUPLICATE REMOVE L39 (10 DUPLICATES REMOVED)
L41 2043 S (STAVROPOULOS, ?)/IN,AU OR (STRATHDEE, ?)/IN,AU
L42 14 S (STAVROPOULOS, ?)/IN,AU AND (STRATHDEE, ?)/IN,AU
L43 4 S L41 AND L24
L44 1 DUPLICATE REMOVE L43 (3 DUPLICATES REMOVED)
L45 39 S L41 AND L10

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L46          35 S L45 NOT L43
L47          18 DUPLICATE REMOVE L46 (17 DUPLICATES REMOVED)

=> S L8 AND ADENOVIR?
L48          55 L8 AND ADENOVIR?

=> S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L41
L49           0 (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L41

=> D HIS

     (FILE 'HOME' ENTERED AT 09:26:33 ON 09 FEB 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 09:26:53 ON 09 FEB 2005
L1           802 S (KOSZINOWSKI, ?)/IN,AU
L2           537 S (MESSERLE, ?)/IN,AU
L3          5359 S (BRUNE, ?)/IN,AU
L4         43708 S (HAHN, ?)/IN,AU
L5             7 S L1 AND L2 AND L3 AND L4
L6             3 DUPLICATE REMOVE L5 (4 DUPLICATES REMOVED)
L7         50178 S L1 OR L2 OR L3 OR L4
L8          5817 S (BACTERIA? (S) ARTIFICIAL (S) CHROMOSOME)
L9         16997 S BAC OR L8
L10       381914 S (PSEUDORABIES OR (GAMMA (2W) HERPESVIR?) OR HERPESVIR? OR CYT
L11          387 S L8 AND L10
L12           82 S L11 AND L7
L13        27515 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L10
L14          207 S L13 AND L8
L15           60 S L14 AND L7
L16           24 DUPLICATE REMOVE L15 (36 DUPLICATES REMOVED)
L17           22 S L12 NOT L15
L18           12 DUPLICATE REMOVE L17 (10 DUPLICATES REMOVED)
L19          305 S L11 NOT L12
L20            5 S (MOSS, ?)/IN,AU AND (DOMI, ?)/IN,AU
L21            2 DUPLICATE REMOVE L20 (3 DUPLICATES REMOVED)
L22        33498 S (MOSS, ?)/IN,AU OR  (DOMI, ?)/IN,AU
L23            0 S L19 AND L22
L24          557 S L9 AND L10
L25           93 S L24 AND L7
L26           11 S L25 NOT L12
L27            4 DUPLICATE REMOVE L26 (7 DUPLICATES REMOVED)
L28            0 S L22 AND L24
L29          464 S L24 NOT L25
L30         3618 S (HORSBURGH, ?)/IN,AU OR (QIANG, ?)/IN,AU OR (TUFARO, ?)/IN,AU
L31            7 S L30 AND L29
L32            4 DUPLICATE REMOVE L31 (3 DUPLICATES REMOVED)
L33            7 S L24 AND L30
L34         6767 S (DELECLUSE, ?)/IN,AU OR (HILSENDEGEN, ?)/IN,AU OR (PICH, ?)/I
L35            4 S L34 AND L24
L36            1 DUPLICATE REMOVE L35 (3 DUPLICATES REMOVED)
L37           55 S  (HAMMERSCHMIDT, ?)/IN,AU AND ((BRIELMEIER, ?)/IN,AU OR (KILG
L38           34 S L37 AND L10
L39           24 S L38 AND PY<1999
L40           14 DUPLICATE REMOVE L39 (10 DUPLICATES REMOVED)
L41         2043 S (STAVROPOULOS, ?)/IN,AU OR (STRATHDEE, ?)/IN,AU
L42           14 S (STAVROPOULOS, ?)/IN,AU AND (STRATHDEE, ?)/IN,AU
L43            4 S L41 AND L24
L44            1 DUPLICATE REMOVE L43 (3 DUPLICATES REMOVED)
L45           39 S L41 AND L10
L46           35 S L45 NOT L43
L47           18 DUPLICATE REMOVE L46 (17 DUPLICATES REMOVED)
L48           55 S L8 AND ADENOVIR?
L49            0 S (WHOLE OR COMPLETE OR ENTIRE OR INFECTIOUS OR GENOME) (S) L4
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